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SOME SOCIAL AND ECONOMIC ASPECTS OF DRUG ADDICTION

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SENSATIONAL headlines, playing up occasional newsworthy episodes, topped off with highly dramatized stage and screen presentations of some people's ideas of underworld life, have, in the last year or so, contributed to growing apprehension that narcotic addiction is rife in Canada, that our very national welfare is imperilled by nefarious and unrestrained dope trafficking.

Actually, of course, such incidents would not make headlines or thriller material unless they were rare, and it is only when drugs get out of hand and become factors in crime and debauchery rather than in professional use for the relief of human suffering that interest is aroused, and the spotlight of publicity is turned upon them.

It is true that we have a narcotic problem in Canada, and that we have our share of public enemies who handle narcotics recklessly. Nevertheless, police authorities and Governmental officials are doing a splendid job in preventing this country from being undermined morally and economically by the unscrupulous activities of those engaged in this nefarious traffic, and are responsible for the fact that the number of Canadians dragged down by the drug habit is only a fraction of our total population.

In Canada today, there are between three and four thousand known drug addicts; more than two thousand of them have come to the attention of enforcement authorities by being involved in violations of the Opium and Narcotic Drug Act. The balance, while not yet convicted of any narcotic offence, are definitely known to be addicts, and in some cases to be engaged in illicit drug trafficking. At the present moment we have close to one hundred cases before the courts throughout the country in relation to narcotic offences.

During the past three years, more than one thousand convictions have been obtained in this country from coast to coast for violations of the Opium and Narcotic Drug Act. This number includes cases against professional personnel, but in the past year, we only found it necessary to bring court action against four practising physicians in Canada. This extremely satisfactory state of affairs in relation to the medical profession, we appreciate, is due in no small measure to the splendid co-operation which we are receiving, not only from the profession in general, but from the executive officers and registrars of the various provincial Colleges of Physicians and Surgeons.

No one knows better than the physician, the latent powers of narcotics for both good and evil. From his own experience, he understands their important contribution to the relief of pain and suffering. If he has no personal acquaintanceship with the more sinister side of the problem, he has certainly read about, and seen motion pictures dealing with, the instrumentality of drugs as destroyers of souls and torturers of human minds and bodies.

In the hands of the criminal, narcotic drugs can create a poisonous traffic which unquestionably infects and corrupts every field of international enterprise and pollutes every stream of human life with which it comes in contact. The habitual use of narcotic drugs by a criminal acts as an incentive to the commission of crime and this, in addition to instigation of more serious crimes, contributes to the difficulties of law enforcement.

Canada has always been alive to the need for keeping close check on narcotics, and this country contributes to international machinery for ensuring that such dangerous drugs be-

come *available only to those who would use them for human betterment.*

Since misuse of narcotics strikes directly at the health and welfare of our people, and because of the scope and the magnitude of the problem, control of potent drugs is accepted as a Federal responsibility. It is directed by the Narcotic Control Division of the Department of National Health and Welfare, which works with the Royal Canadian Mounted Police in enforcement of the Act designed to keep drugs in legitimate channels, and which co-operates with the Department's own scientists in the Food and Drug Laboratories, for the necessary technical investigations and analyses.

Today the problem of narcotics is being tackled by Canada as never before. The Federal Government, in collaboration with provincial and municipal authorities, is bringing every scientific weapon to bear on the matter, and is striving to rescue those already in the toils of the drug habit. Since suppression of illicit trafficking in drugs is the most immediate—if not the basic—problem, enforcement agencies have been brought together to study co-operative operations calculated to uncover and to clean up cesspools of smuggling and peddling.

While combating the drug traffic itself, Canada now plans action in still another direction—an effort to undo the harm which narcotics have caused, and, as far as possible, to rescue and rehabilitate those who are already addicted to drugs.

Some time ago the Government set up a Technical Advisory Committee on Narcotic Drug Addiction. This body, under the chairmanship of the Deputy Minister of National Health, Dr. G. D. W. Cameron, is composed of representatives of the Department of Justice, including its enforcement agency, the Royal Canadian Mounted Police, and its Penitentiaries Branch, and of key officers of the Health and Welfare Department.

This Committee had an exhaustive report prepared on the extent of drug addiction in Canada. The report showed that the habitual use of narcotics by addicts acted as an incentive to the commission of crime of increasing violence and, in addition, occasioned enormous economic loss, through thefts enabling addicts to secure funds to feed their cravings. It was estimated that thefts of narcotics and other merchandise by addicts have been costing merchants of one Canadian city alone more than $3,000,000.00 a year!

Some other startling calculations were made for the Committee. Do you know that an ounce of heroin, worth approximately $11.00 in legal channels, has a value of some $20.00 per *grain* in the underworld? Since there are about 437½ grains of heroin in an ounce of that narcotic, the $11.00 worth of drug, therefore, fetches no less than *$8,750.00* in illicit channels.

Since drugs, too, are normally adulterated by traffickers, the cost to the addicts is considerably higher than even that fantastic figure. And, remember, one grain per day is considered a low stabilizing dosage for an addict.

An ominous observation of the Addiction Report was that more than 50% of narcotic offenders have had two or more previous convictions for a narcotic offence, or for some other violation of the law. In other words, these people are *confirmed criminals.*

You will see, then that Canada must do its utmost to stamp out illicit trading in dope—to clean up its narcotic house. Drug addiction is not only having a devastating effect on human beings—it is draining the life-blood from business. Far more dangerous than the individual addicts or drug traffickers, of course, are the organized bands which carry out elaborate and carefully-planned raids on stocks of narcotics. You have all read of thefts of drugs from stores, hospitals and even from doctors' automobiles.

The answer to such depredations is, naturally, a general tightening of security measures in the handling of narcotics. As long as there are addicts, there will be those who make it their business—and a profitable one it is—to furnish them with the drugs they crave. Such traffickers, almost without exception, are of the criminal classes, which accounts for the close liaison maintained by my Department with other Federal enforcement authorities.

It must be realized, of course, that control of narcotics in this country, and throughout the world, is not simply a police matter. Narcotics have an important legitimate function in contributing to human well-being and the advancement of medical science. It is essential that narcotics, and other drugs, be made available, when and where they are required and, by the same token, they must be kept out of the hands of those who would do mischief with them. By

organization, legislation and efficient administration, Canada is doing her full share in the international regulation of this potent weapon.

Time does not permit me to deal with the day by day narcotic problems insofar as the medical profession is concerned, but there are one or two matters which I must briefly bring to your attention.

In collaboration with the National Film Board and the Royal Canadian Mounted Police, my Department has sponsored the production of a film entitled "Drug Addict". This is now being extensively used as a visual aid in educational and law enforcement training. It shows various systems used in the distribution and administration of narcotics and generally emphasizes for the benefit of selected groups concerned with health, welfare, and law, the evil of drug addiction. The film stresses the theory that addiction *per se* is a medical as well as an enforcement problem and that more attention should be paid to rehabilitation without depreciating the importance of adequate control.

Another important development in the field of narcotic control has been a training program for enforcement personnel and the preparation of lecture material to university undergraduate medical students, colleges of pharmacy and other interested groups. This training program has been carried on during the past three years and has proved itself to be a worthwhile effort in informing the medical practitioner of tomorrow of the narcotic problems of today. Further, special courses of instruction have been organized for R.C.M.P. personnel assigned to narcotic duties, such courses being carried out at the head office of the Department at Ottawa.

Then there is the appalling problem of the new synthetic drugs, which can be prepared with such ease, that the whole line of international control procedure, which had been based mainly on the opium problem, may well have to be revised. Many of these new synthetic drugs have definite addiction-sustaining potentialities and considerable investigation and research is being carried on in this field by the Department's own scientists in the Food and Drugs Laboratories.

One other matter which has caused the Department a certain amount of concern is the personal use of narcotics by some physicians and the increasing number of cases of personal addiction which have come to our attention during the past three years. When we encounter cases of this nature, we endeavour to handle them as discreetly as possible in a purely constructive way, in an endeavour to have the addiction cease, and it is gratifying to be able to report that there are many members of the medical profession in Canada who, although previously addicted, are now leading normal lives and have been doing so for many years, as the results of our efforts on their behalf. I must, however, issue one word of warning to the profession in general. If you are ever confronted with a personal addiction problem, immediately consult the Division of Narcotic Control. We will try to help you if at all possible. Always bear in mind that a very close check is maintained over every physician's purchases and disbursements, and failure to disclose a problem of this nature can have very serious end results to the physician concerned, particularly if restrictive measures have to be officially enforced, and the matter brought to the attention of the provincial College of Physicians and Surgeons.

Finally, there is the question of trafficking in narcotic drugs by some physicians. It is not a difficult matter, provided care is taken, to differentiate between the honest physician who is making a mistake and one who is deliberately trafficking. Many such physicians have no idea that a considerable portion of the drugs made available over their signatures, is in fact, and to our knowledge, not taken by the patient, but after such addict's own needs are satisfied, sold to other addicts at a huge profit. From such source comes the price of the next prescription.

Unfortunately, the potential profit from the illegal sale of narcotic drugs proves to be an irresistible temptation to certain members of the professions who legitimately handle narcotic drugs. In one such instance when protest was made by the addict-customer at the huge price demanded, he was told by the physician concerned, "That is what it costs you outside, and when that outside price comes down, mine will too." I believe that that type of thing is viciously criminal and that the decent and honourable members of the medical profesion are with us in our efforts to put men like that where they belong. Thank Heaven, the proportion of physicians in that category is extremely small.

As to the use to which narcotics can be put legally, Dr. John Amyot, some sixteen years ago, when he was Deputy Minister of Health at Ottawa, stated "Practice legitimate medicine and

you need not even think of the law''. These words are every bit as true today.

In conclusion, I trust that in this short discussion of some of the social and economic aspects of the problem of drug addiction I have been able to show you briefly the complexity of the subject and to point to the possibility of further effective action through adequate treatment in some cases at least. Who knows but what hundreds of erstwhile drug addicts and many thousands of our people who suffer as the result of this scourge may yet look back to the project which we have in mind as an historic undertaking in which Canada took still another step towards securing true national health and welfare. Such action will, I believe, be definitely worthwhile in view of the social loss on the one hand, and the financial loss on the other. My Division, which is charged with the administration of a most important piece of national legislation, designed for the security and welfare of the people of Canada, is fully conscious of the job which must be done. The members of the medical profession are faced with tremendous responsibilities and with their help we will continue to tackle this problem, and I feel quite confident that we will be successful.

ASPECTS SOCIAUX ET ECONOMIQUES DE LA TOXICOMANIE

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S'IL faut en croire des manchettes sensationnelles qui apparaissent périodiquement, ainsi que des pièces de théâtre et pellicules cinématographiques illustrant à leur façon le monde des apaches, on serait porté à croire que la toxicomanie règne en souveraine au Canada et que le traffic libre des drogues est en train de mettre en danger notre bien-être national même. En réalité, une telle publicité ne porte que sur des accidents rares et seulement lorsqu'ils conduisent au crime et à la débauche; on n'en pare guère quand l'usage des drogues se fait à la seule fin d'apaiser la souffrance humaine.

Sans doute avons-nous ici au Canada des tristes individus qui font ce commerce éhonté, mais le nombre de leurs victimes ne représente en somme qu'une infime fraction de notre population, et ce grâce à la vigilance de la police et du personnel de notre Division.

On compte aujourd'hui dans notre pays quelque trois à quatre mille toxicomanes reconnus, la moitié d'entre aux étant déjà à notre connaissance entrés en contravention avec la Loi de l'Opium et des Narcotiques. Il n'en n'est pas de même des autres, bien que nous sachions qu'ils se livrent au commerce des stupéfiants ou qu'ils en usent eux-mêmes. Quelque cent individus sont présentement en instance de justice pour avoir violé la loi; au cours des trois dernières années, plus de mille condamnations ont été effectuées. Fait très consolant à noter cependant, et qui démontre bien la belle coopération de la profession médicale et de nos Collèges des Médecins et Chirurgiens, seulement quatre praticiens canadiens se sont vus traduits devant les tribunaux.

Nul mieux que le médecin, même s'il n'en a pas fait lui-même l'expérience, n'est en mesure de faire la part du bien et du mal imputable à l'usage ou à l'abus des stupéfiants. Il n'en n'est plus ainsi du criminel qui sous leur influence devient porté à commettre des méfaits de plus en plus sérieux, raison de plus pour rendre plus malaisée la mise en vigueur de la loi. Aussi notre pays fait-il sa part, conjointement avec tous les autres pays de l'univers, pour restreintre l'usage des stupéfiants *à ceux-là seulement qui s'en serviraient pour le soulagement de l'humanité.*

Relevant du Fédéral à cause de sa portée nationale et pour le bien-être de toute notre population, le contrôle des stupéfiants est sous la direction de la Division du même nom au Ministère de la Santé et du Bien-Etre Social, de concert avec la Police Montée Royale Canadienne et avec accès à nos Laboratoires des Aliments et Remèdes.

Plus que jamais le Gouvernement Fédéral, en collaboration avec les autorités provinciales et municipales, use de tout son arsenal scientifique, non seulement pour faire cesser le commerce illégitime des drogues mais aussi pour tenter de réhabilitér les malheureuses victimes.

Un Comité d'Aviseurs Techniques formé à cet effet a fait d'importantes révélations au sujet de la vague croissante de crimes ainsi que des vols soit de drogues ou d'argent imputables aux désirs insatiables des adonnés. Ainsi, dans une seule ville canadienne ces vols ont coûté à ses marchants plus de $3,000,000. par année! On ne sait sans doute pas qu'une once d'héroïne,

qui coûte normalement $11.00, se détaille dans le monde des apaches à raison de $20.00 le *grain*, ce qui en porte le coût à pas moins de *$8,750.00* l'once! A un grain par jour, dose considérée faible pour un adonné à la drogue qui est le plus souvent adultérée, l'habitude peut s'avérer nettement prohibitive.

Etant donné que la moitié des individus, par suite d'offenses répétées, sont des *criminels endurcis*, le Canada se doit d'en faire méthodiquement l'élimination, et davantage quand il s'agit de bandes organisées qui pratiquent des vols en bloc dans les magasins, entrepôts, hôpitaux et dans les automobiles des médecins. C'est pourquoi il importe de resserrer les mesures de sécurité dans le maniement des narcotiques et c'est ce à quoi s'occupe mon département de concert avec les autres agences fédérales chargées de la mise en exécution de la loi. Cependant l'intervention policière seule ne résoudra point le problème, car il ne suffit pas simplement d'empêcher les narcotiques de tomber entre les mains de malfaiteurs, il est essentiel qu'ils restent disponibles aux médecins pour contribuer au bien-être de l'homme et à l'avancement de la science médicale.

Pour faciliter l'éducation et l'entraînement du personnel préposé à l'application de la loi par l'image visuelle, mon Département, aidé de l'Office National du Film et de la Police Montée, a régi la production d'un film intitulé "Toxicomane". Montrant les différentes méthodes en cours pour la distribution et l'administration des narcotiques, ce film souligne que la toxicomanie *en soi* est un problème médical aussi bien qu'une mesure policière, et qu'il est tout aussi important de réhabiliter l'individu que de contrôler son commerce illicite.

A cet effet, un programme d'entraînement est en cours depuis trois ans que s'adresse aux étudiants en médecine et en pharmacie et autres groupes connexes, tant il importe de renseigner nos professionnels de demain sur les problèmes narcotiques d'aujourd'hui.

Il se présente à l'heure actuelle un problème d'envergure, celui des drogues synthétiques dont la préparation est si facile, et qui se complique du fait que la procédure en cours concernant le contrôle international des drogues avait principalement trait à l'opium. Il est reconnu que plusieurs de ces drogues synthétiques peuvent conduire à la toxicomanie et à l'accoutumance, et l'on fait à ce sujet des recherches très étendues dans nos Laboratoires des Aliments et des Drogues.

Enfin la question de l'usage personnel des stupéfiants par certains médecins et de leur nombre croissant ne laisse pas de nous causer quelques inquiétudes depuis les trois dernières années. Devant de tels cas, c'est notre pratique d'user de toute la discrétion possible et de faire tout en notre pouvoir pour faire cesser l'accoutumance, et il nous fait plaisir de souligner les succès que nous avons ainsi obtenus dans nos efforts. Mais ici je dois donner un avertissement à la profession médicale. Les achats et les déboursés de chaque médecin sont soigneusement enregistrés, en sorte que le médecin qui fait effraction à la loi s'éxpose à des pénalités et son cas est porté à l'attention de son Collège des Médecins et Chirurgiens.

Quant aux médecins qui pratiquent le commerce des stupéfiants, il y a lieu de différencier ceux qui le font sciemment des autres professionnels honnêtes dont l'excuse est de se tromper. Ces derniers, en prescrivant une drogue, ne peuvent savoir dans quelle proportion leur patient narcomane en usera ni s'il n'en restera pas une part considérable pouvant être vendue à d'autres adonnés à un profit exorbitant.

C'est ce profit facile, démesuré, qui peut tenter de façon irrésistible certains membres de professions qui ont le droit de manier légalement les stupéfiants. Heureusement que la proportion de médecins dans cette catégorie est extrêmement réduite, car ce sont là de dangereux criminels dont la place est toute indiquée derrière les barreaux d'une prison. Quant à ceux qui pratiquent la médecins d'une façon légitime, ils n'ont pas à s'inquiéter car la loi, qui est faite aussi pour eux, ne saurait les atteindre.

Pour résumer ma pensée enfin sur ce problème complexe des narcotiques, je crois sincèrement que grâce à un traitement approprié il nous sera possible de guérir un grande nombre de cas. Le projet qui est présentement à l'étude fera époque au Canada et sera pour beaucoup dans la lutte contre un fléau social qui résulte d'autre part en de lourdes pértes financières. Cependant, avec l'aide de la profession médicale que nous savons à l'avance acquise, notre Division a pleinement confiance d'assurer à toute la population du Canada la sécurité et le bien-être qu'elle mérite.

SOME RECENT CHANGES IN CLINICAL NEUROLOGY*

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SEARCHING for a theme of general neurological interest for this presidential address made me realize that advances in medical knowledge in a very few recent years have led to some radical changes in clinical neurology. Notable progress has occurred in all the special fields concerned with the study of the central nervous system, neurophysiology, neuropathology and neuroanatomy, as well as clinical neurology, neurosurgery and psychiatry. With few exceptions the major developments in any one of these special directions have had their impacts on each other and on the whole neurological corner of the medical globe. An attempt to deal exhaustively with all these related scientific advances would be far too ambitious and it is my intention only to recount some personal impressions of changes apparent to the clinical neurologist during the past fifteen years.

An outstanding contribution to neurological diagnosis and treatment was the surgical discovery of Mixter and Barr in 1934, that ruptured intervertebral discs are a common cause of sciatica. Neurologists with their traditional views about sciatic neuritis being the common cause of sciatica were generally slower than their neurosurgical colleagues in appreciating the importance and truth of this discovery. About 1937 when Dr. K. G. McKenzie told me he thought these disc lesions were the usual cause of sciatica, I can well recall my disbelief and confident arguments in support of sciatic neuritis. Moreover, Dr. McKenzie had the temerity to challenge the existence of chronic brachial neuritis, suggesting that ruptured cervical intervertebral discs were the likely cause of that syndrome. Within a year or two I had climbed on the disc band wagon driven by the surgeons. In 1941 a review of the first one hundred cases of sciatica admitted to No. 1 Canadian Neurological Hospital in Basingstoke produced strong evidence that over 80% were due to herniated intervertebral discs. By then we had come to the stage of considering sciatic neuritis a pretty doubtful and perhaps mythical entity. In subsequent years many of us have come to believe that cervical intervertebral disc protrusions play the same common rôle in causing neck and arm pains as do the lumbar disc lesions in causing low back pain and sciatica. Chronic brachial neuritis has become overshadowed as another neurological myth. It is only fair to add that older neurological studies, notably those of Déjerine in 1914, had shown that most cases of sciatica were due to disease of the nerve roots rather than the nerve trunk. Isolated surgical observations and the pathological studies of Schmorl paved the way for the final important clinical discovery of Mixter and Barr.

There are numerous examples in medical history of erroneous, sometimes ridiculous theories which were subsequently supplanted by correct knowledge based on factual studies. Though destructive thinking alone is not very progressive, we should be on the alert to avoid dogma and confidence in accepting theories about diseases of unknown etiology. Neurology retains a fair share of such diseases in which the cause remains unknown. In a fairly recent book, "The Natural History of Nonsense", Bergen Evans ridiculed many of the prevalent false lay beliefs of the gullible public. In a clever and witty way he discussed the sentimental and unreasonable perpetuation of various unfounded beliefs in regard to animal and bird behaviour, racial customs, diets and so on. It might be possible to write a similar critique about some of the complacent beliefs persisting in medicine. Whenever possible we must replace neurological nonsense with proved sense. It was well phrased by Sir Heneage Ogilvie recently: "The orthodoxy of today is the heterodoxy of yesterday and may be the discarded fallacy of tomorrow".

Epilepsy is one of the neurological interests which has been the subject of considerable change in recent years. A major therapeutic advance was made when diphenyl hydantionate was introduced by Merritt and Putnam and this led to the discovery of other valuable anticonvulsant drugs. Studies of the exposed human cerebral cortex as pioneered by Wilder Penfield have contributed important data of direct clinical applicability. Electroencephalography has vastly refined our diagnosis and

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treatment of convulsive disorders. It has allowed a verification and extension of Hughlings Jackson's far-seeing clinical deductions about epilepsy and the cerebral cortex. The intriguing more complicated seizures with alterations of ideation, consciousness, speech, special senses and visceral function are now approachable by more precise clinical and electrical study and correlation. Newer biochemical and electrophysiological studies even give some promise of eventual understanding of the fundamental nature of the epileptic discharge.

Electroencephalography has become a practical and necessary diagnostic aid in the modern clinical neurological department. Though this relatively new technique remains primarily an investigative method, it has become valuable as another ancillary aid in the diagnosis and assessment of brain tumours, brain injuries, encephalitis and brain abscess, as well as its particular importance in epilepsy. The accuracy and value of electroencephalography to the clinician depends in considerable degree on his own knowledge and interest in the subject. Like other special diagnostic procedures it can be used safely and accurately only when viewed in the full perspective of the complete clinical and laboratory evidence. It would seem essential that the neurologist should have a working knowledge of the interpretation of E.E.G. tracings and should look at the actual record as well as the written report from the electroencephalographer. Used in this way the electroencephalogram may come to occupy a position in neurology approaching that of the electrocardiogram in cardiology. Such practical diagnostic applications need not detract from the important value of the method as a research tool.

One of the most striking therapeutic advances in my experience has been the treatment of meningitis by antibiotics. Most of us have had experiences within our own families to dramatize the appreciation of these newer life-saving drugs. Well can I picture as a medical student memorizing the list of bacterial types of meningitis with the mortality percentages of each. With the exception of meningococcal meningitis in which serum had proved of value, the mortality rate was over 95% in those few types where it was not 100%. The dramatic improvement in results of treatment of this terrible group of diseases is well known. Significant advances were made with the sulfonamides, then still greater results were achieved with penicillin. Streptomycin has enabled successful treatment of many of the less common cases of meningitis due to Gram-negative bacilli. Even tuberculous meningitis, the worst of all, has been tackled with some success by streptomycin. Nowadays one approaches with enthusiasm and hope the treatment of cases of acute purulent meningitis; just a few years ago one felt helpless and dismayed by the same diseases. The treatment of virus infections of the nervous system remains a largely unsolved problem. In the period under review there have been several advances in virus studies such as the improved knowledge of the polio virus and the work of Armstrong on the choriomeningitis virus. Perhaps the stage is already set for important discoveries in this fairly large field of virus infections of the nervous system.

Penicillin has radically changed the neurological scene in regard to the treatment of neurosyphilis. The fever cabinet, the malarial mosquito, and the arsenic molecule are being rejected like the blacksmith and the chimney sweep and are threatened with total unemployment.

Other less spectacular, but valuable and stimulating advances have been made in the field of neurological therapy. Dr. Mary Walker's observation on the specificity of prostigmine for myasthenic symptoms was a practical contribution to treatment and also stimulated considerable important physiological study of the acetylcholine, cholinesterase and eserine story. It is of interest that Dr. Walker's original trial of eserine in myasthenia was based on the observation that myasthenic symptoms resembled those of curare poisoning. In the more recent renewal of interest in the thymus gland in myasthenia, a popular theory has been that the thymus may give off a curare-like toxin in this disease. The value of thymectomy for myasthenia is under current surveillance and at present opinions are not entirely uniform. At best it seems that thymectomy will prove curative for only a small portion of myasthenics and it is hoped that some new means may be discovered for selecting suitable cases for surgery. The discovery of the efficacy of quinine for myotonia was another finding of some therapeutic value and considerable

physiological interest. Allott's observation that serum potassium was lowered in attacks of familial periodic paralysis was another important contribution in the early part of the period under review. Dr. Donald McEachern and his colleagues have contributed several important studies to this whole promising and interesting field of neurochemistry and neuromuscular diseases.

Interest in the nutritional aspects of disease of the nervous system has been actively fostered in recent years by scientific projects as well as by enthusiastic pharmaceutical firms. The rôle of thiamine deficiency in Wernicke's encephalopathy and alcoholic neuritis has been fairly well established. Starvation conditions amongst prisoners during the war produced a large number of neurological disorders of nutritional basis including beri beri and other less known syndromes. The discovery that vitamin B_{12} is the factor related to subacute combined degeneration of pernicious anæmia is another important discovery. Experimental work gave some promise of a vitamin E rôle in muscular diseases, though little if any confirmation or practical application has yet developed.

Progress in the field of cranial arterial diseases has come about through several different approaches. Continued use of ergotamine tartrate for migraine has established its merit and has aided in the understanding of the mechanism of headache. The studies of Wolff and his collaborators have significantly advanced knowledge of this common symptom of headache. Horton's writings on a special type of vascular headache have drawn attention to a particular syndrome as well as pointing to a possible histamine basis. The clinical and pathological nature of temporal arteritis has become better understood. The neurological complications of periarteritis nodosa and lupus erythematosa have also received better recognition. The conception of a group of collagen diseases including these types of arteritis has been of considerable interest to the neurologist as well as the general physician.

The past few years has seen a revived interest in cerebral arteriography with the development of a simplified percutaneous method. This has focussed attention on intracranial aneurysms with renewed consideration of surgical treatment. Certainly there is no room for complacency in our present methods for dealing with the profuse dangerous bleeding from a large artery at the base of the brain in such cases of aneurysm. This is an obvious challenge which neurosurgery has accepted with commendable enthusiasm. In the series of cases studied and followed by Hyland and myself, the mortality was high in the acute stages of hæmorrhage, but the danger of late recurrences seemed relatively low. We feel that the place for any possible surgery is primarily in the acute stage of hæmorrhage from an aneurysm, and that in the quiescent healed stage it is usually wiser to rest content with the kindness of nature. The next few years will probably see more consolidation of opinion in this difficult problem, as well as some further improvements in surgical technique.

Electroconvulsive therapy and frontal lobotomy for mental disorders can be considered as important developments in high level neurology. Though the deliberate production of major convulsions for depressive states seems a distasteful and crude innovation, it has proved a helpful and justifiable procedure. Certainly it has favourably altered the stringent program of hospital confinement forced upon those unfortunate patients with acute melancholic illnesses. Scores of persons so afflicted are now remedied by short periods of general hospital care, who previously would have required lengthy admissions to mental hospitals. Frontal lobotomy seems to be standing the test of time as another radical crude cerebral approach to mental illness. Both of these physical neurological types of psychiatric treatment have stimulated a great deal of interest and investigation into the more complex brain functions. Undoubtedly the methods of therapy will be replaced by more precise and gentle measures, but their demonstrated value throws light ahead with sufficient illumination to suggest that the paths are in the right direction.

In reminiscing about these radical changes affecting clinical neurology in the past fifteen years, it would be remiss to avoid some mention of the last World War period. Particularly worthy of recall is the fact that the Royal Canadian Army Medical Corps sent overseas in the first year of the war a hospital well staffed and equipped to handle neurosurgical, psychi-

atric and neurological cases. This developed into a fairly large overseas base hospital in which all those concerned with treating disorders of the nervous system worked co-operatively and effectively in one compact unit. Tribute should be paid to those who had the foresight to initiate and organize No. 1 Canadian Neurological Hospital, chief amongst whom were Dr. Colin Russel and Dr. William Cone. From every possible practical standpoint this hospital proved a success which was often commented upon and even envied by visiting British and American colleagues. Those of us who had the good fortune to serve with this hospital were left with an indelible impression of the good team work attained between neurosurgeons, psychiatrists and neurologists.

Perhaps the greatest clinical contribution to neurology during the war was the treatment of infected head wounds by penicillin. The war also produced important clinical studies of head injuries and stimulated valuable research such as that of Denny-Brown and Ritchie Russell on concussion. The various studies on blast effects from high explosives tended to show that the central nervous system was particularly immune from physical damage due to blast. So much was done and written about war neuroses that no attempt will be made to review that subject fully. Notable in the handling of functional nervous disease was a broader attitude with emphasis on the background personality as well as the particular reaction produced by war stress. Physical adjuncts such as continuous narcosis and subcoma insulin were fully utilized in the treatment of neuroses. There was some progress in practical administrative arrangements for grading and special employment of neurotics and psychopaths. Many lessons were learned and much remains to be learned about both therapeutic and administrative aspects of this major problem of military medicine. In D.V.A. work since the war it has been possible to gain a few impressions about the efficacy of the policy and methods used in regard to neuroses overseas during the war. Certainly pensions consideration of these cases has been facilitated by the full biographic histories recorded. The number of battle exhaustion cases requiring subsequent treatment at home has seemed minimal and much lower than earlier anticipated.

SUMMARY

The subjects mentioned in regard to developments in clinical neurology have been—intervertebral discs, epilepsy and electroencephalography, antibiotic drugs, neuromuscular and nutritional diseases, headache and arterial diseases, angiography and intracranial aneurysms, electroconvulsive therapy and lobotomy, and military neurology. The comments have been brief and superficial and many important clinical and research topics have been omitted. However, the subject matter is illustrative of some of the radical progress and invigoration of neurology in recent years. The material might also serve as a basis for a few concluding remarks concerning organization and development of clinical neurology in the future.

The discoveries mentioned have come from scattered directions both within and without the arbitrary bounds of neurological sciences and doctrines. An obvious implication of the contributions by physics, chemistry, general medicine and surgery is that neurology must not be too isolated. There are intricate ties with general medicine and surgery and there must be close liaison with basic sciences.

Other subjects mentioned illustrate the increasing intricacy and extent of technical diagnostic and investigative procedures. Still more special techniques not mentioned are electromyography, electroencephalographic recording from the exposed brain and the common radiological procedures such as pneumoencephalography and myelography. Allied departments of neuropathology, neurophysiology and neuroanatomy also have their special procedures. The clinical neurologist must constantly think and talk in terms of anatomy, physiology and pathology so that his relationship with these laboratories requires continued intimacy. Because of these questions of equipment and procedures as well as the common merging interests there are obvious advantages in close organization and teamwork between neurology, neurosurgery and psychiatry. Each of these related specialties requires similar liaison with the laboratories concerned with brain function and disease.

Neurology has so many merging interests with other clinical subjects that there are various alternative methods of organization within the medical school. A university may choose to arrange neurology as a combined department with neurosurgery or psychiatry, as

a subdivision of general medicine or as an independent department. In some measure this choice of organization will determine whether the aims of neurology are best fostered in the direction of undergraduate teaching, postgraduate teaching, diagnosis and treatment of patients, or research. To provide adequately for all these needs a large and wealthy medical school is required and a wise administration sympathetic to the requirements and importance of the departments concerned with diseases of the nervous system.

It hardly needs saying that special techniques and detailed plans of organization are of secondary importance to that of personnel. If this branch of medicine continues to attract men of high calibre, no fears need be held for the future development and status of neurology. Cajal put this thought very well in his words: "For scientific work the means are almost nothing and the man is almost everything".

THE PRACTISING PHYSICIAN IN THE CONTROL OF SYPHILIS*

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AMONG the truly dramatic moments in modern medical history can be included one in October, 1943, when Dr. John F. Mahoney, formerly of the United States Public Health Service, Venereal Disease Research Laboratory, at a meeting of the American Public Health Association, reported the first successful treatment by penicillin of four early cases of syphilis.[1] At the conclusion of his announcement, Dr. Mahoney made this statement, "Should more extensive and prolonged experience confirm the impression which is to be gained from the pilot study, a rebuilding of the structure of syphilis therapy may become necessary".

Since that prediction was made, almost seven years ago, changes have occurred in syphilis management at almost a dizzying pace, certainly one with which the practising physician would find it difficult to keep abreast. However, rather than adding to the confusion which heretofore has surrounded the syphilis patient, the advent of penicillin has, by progressive steps, tended more to resolve it.

This group scarcely need be reminded that prior to Mahoney's discovery the treatment of syphilis had passed through a more or less tangled succession of therapeutic procedures and drugs; originally, the mercurials, followed early in this century by the arsenical compounds, then the bismuth preparations, and more recently various derivatives and combinations of these drugs. In many instances there was marked diversity of opinion as to the efficacy, manner and indications for their use. Each, in addition to its therapeutic action, presented varying degrees of toxicity to the host as well as to the spirochæte, and in some cases the spirochæte proved itself to be considerably more resistant to the drug than the host. As Pelouze has so aptly put it in describing another procedure, the earlier management of syphilis might be regarded as "an ordeal in which many patients go dangerously close to the pearly gates, some hear the hinges creak, and some just stop hearing forever".

In comparing these earlier methods of treatment with modern syphilis therapy, it becomes increasingly apparent that penicillin has, in fact, exerted a clarifying and stabilizing influence, despite the continuing problems relating to its most effective usage. Formerly, there was understandable cause for the busy practitioner, upon encountering a case of syphilis, to retire behind the plea of diagnostic problems, treatment confusion and follow-up difficulties, with the result that not infrequently the patient was either abruptly disposed of or inadequately treated.

As a result of the progress made over the past seven years there is no longer any justification for such a situation. The basic principles of diagnosis and treatment of syphilis are becoming increasingly clearly defined. The fundamental knowledge is now available to the practising physician who should be ready to accept the syphilis patient with all accompanying responsibilities.

Of additional concern to the practitioner is the growing proportion of syphilis patients electing to seek treatment from him rather than

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at the public health clinic. This trend is not, by any means, uniform. It varies in different parts of the country, economic circumstances unquestionably playing a major part. Nevertheless, the tendency is apparent and the patient is turning to the private physician more and more for the treatment of his syphilis infection. This is as it should be, but one cannot help feeling somewhat apprehensive of this development in the over-all control program. One wonders if the practitioner will be sufficiently interested, willing and prepared to accept the full responsibility of the syphilis patient.

The contribution of the practising physician in the syphilis control program centres upon two major features—case-finding and case-treatment. To control syphilis adequate treatment is necessary, but the best treatment in the world is useless unless those suffering with the disease are found and provided with its benefits.

Of the two, discovery and treatment, it is generally conceded that the treatment element is better performed. Dr. Joseph E. Moore of Johns Hopkins University recently asserted[2] that the persistence of syphilis amongst us is due largely to the fact that so many syphilis patients pass completely unrecognized until infection of others or the ultimate break-down of the individual himself has already occurred. Thus, we can only conclude that the *discovery* of the syphilis patient is the key procedure in syphilis control. Let us, therefore, examine this a little more closely.

Case-finding involves two elements, first the correct diagnosis by the physician of patients showing the active lesions of syphilis, and second, the organized effort to search out the infected individual who shows no lesions. As listed by Moore[2] there are three reasons for the relatively unsatisfactory results encountered by the practising physician: (1) The doctor's puritanical state of mind; (2) his failure to realize the prevalence of syphilis; (3) the inaccurate diagnosis of syphilis.

Regarding the first, it has been truthfully said that too many doctors still believe that no one has syphilis but old soldiers and sailors, prostitutes and criminals. They still believe that being well born, socially prominent, morally above reproach, wealthy and well educated eliminates any consideration of infection. They still look upon syphilis as a disgrace and not as a disease. They hesitate to offend their own patients, even to the point of not testing for its presence.

In the second instance, it is not fully appreciated by many that syphilis is a common infection existing in all classes of society. In Canada last year more than 8,000 cases were reported.[3] One wonders how many more were seen but not reported, not to mention the cases not discovered. Many physicians will not accept the fact that syphilis exists at all social levels and the persistence of this belief has produced in the minds of many practitioners what Stokes describes as "a low index of suspicion"—the existence of syphilis being looked upon as incredible.[4] Summing up these thoughts brings to mind the words of Osler in this regard:

> "But I see an incredulous look on some faces and I hear the whispered comment . . . 'tis heard often enough! 'Where is all this syphilis? It does not come my way'. Yes, it does. The syphilis we see, but do not recognize, everywhere awaits diagnosis, so protean are its manifestations."

According to Moore, "the third and most important reason for failure in case-finding lies not in the confusion of morals and medicine, but in the diagnostic inaccuracies of medicine itself". The main point here is that the fundamental diagnostic facts, the simpler principles which should govern diagnosis, have been lost in the maze of detail, the apparent complexity of the syphilis case. In my opinion there is no doubt that this state of mind was initiated during medical student days through numerous instructors presenting from time to time different aspects of the disease and demonstrating a variety of lesions similar to, or attributable to syphilis, and with little correlation. As a result syphilis lost its identity as a specific disease condition and became instead a consistent but rather vague inclusion in the differential diagnosis of a multitude of other ailments.

To counteract this situation which persists in the attitude of many practitioners, we would like to offer certain minimum suggestions in the practical approach to syphilis control. As in so many other diseases, the physician's total responsibility can be reduced to two fundamental procedures—accurate diagnosis and adequate treatment.

First, as to the accurate diagnosis of syphilis, there are three essential principles for the practitioner to observe:[2]

1. *Raise the index of suspicion.* Suspect syphilis at any or all times and take positive steps to confirm or dispel such suspicion. It must be remembered that syphilis is a very prevalent disease.

2. *Appreciate that syphilis is often difficult to diagnose clinically, even by the expert.* Clinical suspicion is easier to arouse than clinical certainty to determine.

3. *Take a blood test.* Clinical suspicion, once aroused, can in most instances be accurately resolved into certainty by the serologic test. In untreated syphilis the serologic test is 95% efficient.

What is the practical application of these principles? In the patient suspected of having syphilis, a few pertinent questions by the physician surely form as much a part of the routine history taking as in any other condition. If the history is suggestive then the patient must be regarded with suspicion until his freedom from infection can be proved. Physical examination, obviously, is the next step. The only comment I would offer here is that, as in all cases, it should be thorough and the physician should be alert to detect and correlate the physical findings. How true it is that so often the patient is *seen* but how unfortunate that he is not *observed.*

With the finding of an open lesion, an ulcer, a sore of any kind, a fissure or even a minute erosion, particularly on or about the genitals, a darkfield examination should be performed. It must be remembered that the diagnosis of primary syphilis is a laboratory and *not* a clinical procedure. Here the darkfield examination is all-important.

It is fully appreciated that there may be difficulties in the physician having the darkfield examination carried out, but wherever possible local facilities should be taken advantage of—hospital laboratories, branches of the provincial laboratory, or a physician with a darkfield microscope, properly trained in its use. Failing these, a capillary tube specimen sent by mail to the central provincial laboratory may provide the answer.

Where a negative darkfield is obtained or where such an examination has not been carried out, the suspicious case should be followed for a period of three months employing the serologic test monthly, as a minimum, préferably every two weeks. Faithfully utilized by the practising physician the blood test will solve innumerable diagnostic problems and contribute greatly to the success of his efforts in syphilis control. In providing facilities for the darkfield examination and the serologic test, the provincial laboratory makes available invaluable diagnostic aids for the practitioner's use. These should be utilized to the fullest extent.

It might be asked, when should serologic tests for syphilis be performed? *Under any circumstances in which an even remote possibility of syphilis may have more than ordinary implications and whenever and wherever syphilis may be suspected.*

The serologic test for syphilis is mandatory in couples contemplating marriage and in the expectant mother. The importance of the premarital and the prenatal blood test cannot be overemphasized. So too in pre-employment examinations, general physical examinations, hospital admissions and similar circumstances, an excellent opportunity is afforded the physician to bring to light unsuspected cases of syphilis. Additionally, any physical ailment in which there exists even the slightest possibility of syphilis demands that a blood test be performed.

Summing up these thoughts on the diagnosis of syphilis we find that our approach can be reduced to three simple steps—*ask—observe—test.* If conscientiously performed, few cases of syphilis will be missed.

While dealing with the discovery of the disease we should consider briefly the public health aspects of the syphilis patient—locating the source of the infection as well as any subsequent contacts. The physician who truly appreciates that all *relevant* contacts must be examined and, wherever necessary, treated, will undertake adequate public health protective measures and can do so with a minimum of effort and time.

How easy it would be, at the time of initial history taking to add a few more questions so vitally important in syphilis control—"Where do you think you got this? What is the name, the address, the description? With whom have you since had contact?" The earlier such questions are asked, the more likely is accurate information to be obtained. And with this information the epidemiologic follow-up will have been initiated.

Several courses of action are open to the doctor in the search for contacts. (1) Have the patient do the epidemiologic work; (2) do it himself; (3) have his provincial health department do it.

The first is the best, especially if the patient is trustworthy and can be depended upon to bring in his contact or contacts for examination. The second I am afraid we must dismiss except, perhaps, in the rare case and under exceptional circumstances. Regarding the third, it should be appreciated that the provincial epidemiologic workers handle all such matters in complete confidence, they are fully dependable and always available. They are efficient, but only in direct proportion to the adequacy of information provided by the physician.

It is immaterial from the point of view of syphilis control who actually performs the epidemiologic work, so long as it *is* done, and done effectively. If the patient will bring in his contact, well and good, but if not, the physician should at least help the provincial health workers by providing adequate information when reporting the case. While "paper work" is objected to strenuously by many physicians, the form prepared for this purpose can be rapidly and easily completed. For syphilis control purposes the information it conveys is invaluable.

TREATMENT

And now to the second major feature in syphilis control—the adequate treatment of the disease. Compared with the complexities which existed in this field up to only a few years ago, treatment today is becoming almost elementary. The basis of all modern syphilis therapy is penicillin and the only variables which are yet encountered relate to the precise amounts of the drug administered, the time interval between doses, duration of treatment and whether or not in certain stages of syphilis other medication should be administered concurrently or following the penicillin schedule. This may seem a somewhat confused picture, but in none of these details are the differences of opinion of any great significance.

At the present time procaine penicillin G in oil, with 2% aluminium monostearate is the preparation of choice in most stages of syphilis. In early syphilis total dosages of from 2,400,000 to 6,000,000 units are recommended, depending upon the individual clinician. Probably the most commonly favoured schedule is a dosage of 600,000 units of procaine penicillin G given every other day, for 10 injections.

According to Moore,[5] a success rate of 85 to 90% may be anticipated at the end of 18 to 24 months' observation, following the administration of 6,000,000 units of procaine penicillin in early syphilis, *i.e.*, primary, secondary and latent syphilis of less than four years' duration. It should be mentioned that the incidence of relapse is rare after the first year following treatment.

In other forms of syphilis, prenatal, congenital and in neurosyphilis the picture is even more favourable. In prenatal syphilis the failure rate encountered following the treatment of several thousand cases is but 1 or 2%. That is, the baby is protected in 98 to 99% of cases of syphilis in pregnancy treated with adequate dosage of penicillin. It has recently been brought out that retreatment of the mother in later pregnancies is not necessary to protect the fetus, three cases only of infantile syphilis having occurred in 390 pregnancies which followed an adequate course of treatment. However, in deciding whether or not treatment is necessary, to be on the safe side the mother should show a negative serologic test or, if positive, it should be of low titre at the time of the subsequent pregnancy.

In congenital syphilis the picture is extremely favourable. With treatment initiated before the third month, cure rates approach 100%. In a large group of infants and children treated with penicillin the relapse rate is reported as approximately 3%. In both syphilis in pregnancy and congenital syphilis water soluble crystalline penicillin G has been strongly recommended.

It has been amply demonstrated that penicillin is even more efficacious in neurosyphilis than in the early stages of the disease. Following treatment, the cerebrospinal fluid findings become normal in 90 to 95% of all patients regardless of the type of neurosyphilis. In the spinal fluid, the cells and protein return to normal within six months after institution of penicillin therapy. The complement fixation test and colloidal gold reaction follow shortly thereafter. These results once obtained appear permanent in 90% of the patients treated. In passing, it is interesting that in neurosyphilis

it has not yet been explained why such favourable results are encountered in spite of the fact that penicillin does not appear to penetrate the central nervous system in the same concentration as in other body tissues.

In cardiovascular syphilis one must be more reserved at this time. It can at least be said that penicillin does no harm. Moore and others have stated that the Herxheimer reaction need not be feared following the use of penicillin in cardiovascular syphilis, but some observers prefer to initiate treatment of such cases with a preliminary course of 6 to 8 weeks' bismuth therapy.

While recent reports are favourable so far as clinical improvement is concerned, it will take several years yet to determine whether penicillin is of appreciable benefit in terms of prolongation of life in cardiovascular syphilis. Pending such findings, it is considered desirable to use penicillin for the treatment of syphilis involving the heart and great vessels in preference to prolonged courses of metal chemotherapy with its attendant toxicity and uncertain results.

With respect to specific treatment schedules and follow-up procedures, the practising physician should ascertain what is recommended in his own province. Treatment outlines in all forms of syphilis, follow-up procedures involving serologic and spinal fluid examinations, consultations on individual patients, free drugs, free laboratory diagnostic aids, these and other services are available from the provincial health department.

Before summing up I would like to refer briefly to what is probably one of the most disturbing incidents in the diagnosis of syphilis —the occurrence of the false positive serologic test. As a result of a number of other disease conditions, usually accompanied by febrile reactions, as well as vaccination, serum injections, etc., a change may occur in the patient's serum, usually transitory in character, which will show a positive serologic reaction *not* due to syphilis. Because of this, treatment should *never* be initiated on the basis of a single positive serologic test without other supportive evidence. At times it is exceedingly difficult to resolve such a situation and only by repeated blood examinations can the true significance of the test be determined, especially in the absence of other clinical, laboratory or historical findings.

However, recent experimental work carried on at Johns Hopkins University indicates that even this problem may be eliminated within the early future. According to findings reported by Nelson and his associates,[6, 7] there exists in the blood of syphilis patients an antibody which exerts a specific effect against *Treponema pallida*. This antibody is distinct from reagin, the detection of which in the serum forms the basis of the Wassermann, Kahn and similar tests. It is found in the cerebrospinal fluid of syphilitic patients as well as the blood serum.

Nelson's method of determining the presence or absence of the syphilitic antibody is under intensive study at present and it will probably be restricted to the research laboratory for some time to come. However, at this moment it can be said that it holds great promise in the differentiation of biologic false positive serologic tests from those actually due to syphilis and, ultimately, may mean the availability of a single, fully reliable test of the serum to establish the existence or otherwise of syphilis.

To sum up, then, what, precisely, is the rôle of the practising physician in the control of syphilis? Expressed in terms of the simplest *principles:* He should suspect syphilis at any or all times; he should inquire, observe and test for syphilis more often than he does; he should treat his known cases adequately and, by follow-up, he should assure himself that the treatment has been effective; he should appreciate that to control syphilis, contacts *must* be found and examined, and he should cooperate in finding them.

Reduced to the minimum *practical* steps to be taken, the physician should: Ask more questions regarding the possibility of syphilis; take more serologic tests for syphilis; treat the syphilis case with penicillin and if there is no better guide available, administer 6,000,000 units of procaine penicillin in doses of 600,000 units every second day; follow-up with serologic tests for syphilis and cerebrospinal fluid examination; report syphilis cases and *above all* report early syphilis contacts.

If every physician would do at least this, minimal though it may be, his contribution to the control of syphilis would be a truly significant one.

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RÉSUMÉ

L'auteur étudie les problèmes que le médecin praticien rencontre losqu'il traite la syphilis. De plus en plus, surtout depuis l'avènement de la pénicilline, le médecin de famille a une plus grande part à jouer dans le dépistage et le traitement de cette maladie. L'auteur établit une ligne de conduite pour porter un diagnostic précis: (1) soupçonner la syphilis en tout tempts; (2) se souvenir que la syphilis est parfois difficile à diagnostiquer même pour un expert; (3) faire une épreuve sérologique. Une fois la syphilis diagnostiquée il faut retrouver les contacts, c'est là que le patient vient en aide au médecin.

Le traitement de la syphilis est bien simplifié depuis quelques années. A la base du traitement moderne se trouve la pénicilline. Actuellement la pénicilline procainée G dans l'huile avec 2% de monostéarate d'aluminium semble être le médicament de choix. La routine la plus fréquente est: 600,000 unités tous les deux jours pour dix injections. D'après Moore on peut s'attendre à 85 à 90% de succès dans la syphilis du début i.e. primaire secondaire et latente de moins de quatre ans. Les rechutes sont rares. Dans la syphilis prénatale les insuccès ne sont que de l'ordre de 1 à 2%. Dans la syphilis congénitale la pénicilline donne presque 100% de succès si le traitement est commencé avant trois mois. Dans la syphilis nerveuse les résultats sont même plus satisfaisants que dans la syphilis primaire. Dans la syphilis cardiovasculaire la pénicilline ne nuit pas et il n'y a pas de danger d'une réaction d'Herxheimer. L'auteur conseille de ne pas commencer le traitement sans avoir deux réactions sérologiques positives. Le médecin doit se faire un devoir re suivre cette ligne de conduite et surtout de rapporter les contacts donnés par le patient.

YVES PRÉVOST

THE MANAGEMENT OF DEPRESSIONS*

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THE diagnosis of "depression" is generally considered to be in the province of psychiatric practice, and at once calls up the typical clinical syndrome of the depressed facies, the hopeless outlook, the self-debasing ideas, the suicidal impulse or act. However, this really describes the psychotic depression alone. Actually, the subtler manifestations of the depressed state are seen in every practitioner's office, disguised by a host of somatic symptoms which obscure the primary mood disturbance.

The chief complaints are disturbed sleep, loss of appetite and weight, fatigue and exhaustion, loss of interest in usual activities, loss of libido and pleasurable affects. The sleep disturbances may involve difficulty in falling asleep, early waking, or restlessness during sleep. Nightmares or anxiety dreams occur, and if available to recall, give useful clues about underlying conflicts. Loss of appetite is associated with loss of taste or perversions in the sense of taste, so that everything is described as bitter, flat, salty or bad tasting. Weight loss is dependent on nutritional changes which result from diminished intake of nourishment coupled with the increased energy demands in the sick person. In severely depressed patients, severe starvation effects may be seen, and tube feedings are sometimes necessary to sustain life.

Fatigue is a regular complaint. It is most marked in the early part of the day and gradually improves as the day wears on. Many patients who are mildly depressed report that they only feel "like themselves" in the evening. This type of fatigue is easily differentiated from the fatigue or organic origin by its special characteristics. Most noted in the a.m., it improves with activity and pleasant distraction, is not relieved by rest and has other associated signs of neurotic stress.

The psychological state of the patient can best be described as one of general inhibition. In the severely ill patient, the inhibition is reflected in psychomotor retardation, blocking of speech and a general poverty of thought. In the milder case, there is simply a lack of drive and initiative, listlessness, inertia and lack of enthusiasm. Usual activities or hobbies no longer interest the patient. Loss of interest in everything and withdrawal from social contacts and pleasurable activities is characteristic. Sexual drive diminishes, frequently to the impotent state. The libido shift is a reliable guide for timing of the onset of the illness and is a good signpost of the recovery process.

The affect (mood) is one of pessimism, moodiness or frank depression. The ability to laugh, smile or enjoy is lost. Brooding and easy tearfulness is noted. The depressed patient feels and behaves as though the world is desolate, and he is lost. Actually, the depressed state has been compared to the normal grief reaction seen in mourning. Here, however, the depression is pathological, either because there is no external stress obvious, or because the reaction far exceeds in severity what is expected from the bereavement or disappointment actually suffered.

Another characteristic in the depressed state is the decrease of ego strength and the (relatively) increased prominence of superego (conscience) activity. Loss of confidence, loss of efficiency, withdrawal from social contacts and

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activity, loss of self-esteem are noted. The superego appears to assume a critical, domineering sadistic attitude towards the ego, which is reflected by feelings of inferiority, self-depreciation and intolerable guilt, from which the patient seeks escape by expiations, self-punishments small and large, surgery (polysurgical addict) or suicide.

The superego behaves towards the "self" (ego) much as the enraged hostile parent behaves towards the guilty and offending child. The ego responds to these pressures by admission of wickedness, confession of guilt, and humble submission to censorship and punishment. The thoughts and feelings of the depressed person are self-condemnatory, with self-blame for behaviour or wishes judged to be sinful, and yet demanding love and forgiveness, in spite of "sins" which are grossly overemphasized or exist only in phantasy. The self-punitive expiatory needs are reflected further in the giving up of pleasure, in giving up of food and in various small or large tortures, or mutilations, the individual appears to compulsively seek out.

Somatic manifestations of the depressed state are reflections of the general inhibition and state of tension present. Dyspepsia, constipation, dysmenorrhœa or amenorrhœa, headaches, generalized aches and pains, fatigue and weight loss are familiar complaints. Functional complaints of every sort occur and may mask the depression. Laboratory findings are not significant in relationship to the clinical picture.

Diagnosis. — The symptom complex outlined above, *i.e.*, insomnia, loss of appetite, fatigue, loss of libido, depressed affect, diminished self-esteem represents the essential features of a depression. It must be pointed out at once, that this does not however, represent a disease, or a disease process, but rather a type of reaction, or specific kind of pathological behaviour response. It is clear that a depression may exist separate from, or coincident with, any organic disease process. The psychosomatic concept emphasizes that any illness process (organic) has its repercussions within the personality structure of the patient, and likewise that personality factors influence the natural life history of the disease. Thus the diagnosis of depression does not necessarily exclude the presence of other illness, either organic or psychological.

Depressed reactions can occur in the life history of any patient suffering from tuberculosis, heart disease, carcinoma, etc. As well, depression may arise as a reaction formation in the history of a manic depressive psychosis, a schizophrenic reaction, anxiety hysteria or obsessive compulsive neurosis. Depressions frequently occur in middle life or at the involutional period. Typically, here, the illness arises on the basis of a rigid long-standing obsessive compulsive neurosis, with gradual failure of the ego to cope with the persistent pathological demands of the neurosis in the face of decreasing physical and emotional stamina.

The precise evaluation of the depressed reaction, in its larger setting within the individual patient, becomes then an important part of diagnosis and in planning therapy.

Depressive equivalents may occur. Most common are bouts of alcoholism, periods of complete anorexia, episodes of exhaustion and nervous fatigue, or circumscribed periods of apparent hypochondriasis. A study of the patient's personality and life stresses will make clear that these symptoms are depressive equivalents.

Etiology and pathogenesis.—The present understanding of the psychological mechanisms operative in the depressed state still rests on the fundamental contributions of Abraham.[1] As a result of his psychoanalytic observations, he pointed out four factors of significance in this reaction.

1. There is a special fixation of the libido (psychic energy) at the oral level. (This refers to that stage of growth in which sucking, biting, chewing and oral pleasures are especially prominent as sources of gratification.) This fixation may be constitutional.

2. There has been a severe injury to infantile narcissism (infantile ego) brought about by successive disappointments in love. (This refers to the child at an early age feeling rejected or unloved by the valued parent, either as the result of death, separation, emotional rejection or replacement by another child for her love.)

3. This initial trauma occurs in the pre-edipal stage of development.

4. The repetition of this primary disappointment in later life acts as the precipitating element in the individual predisposed by the above factors which have distorted his personality development.

The classical stress which produces a depression is either a disappointment in love, or the loss of a loved person through death or separation. However, in predisposed persons,

other disappointments may have an equivalent meaning. Through the loss of self-esteem or personal devaluation, the individual may deem themselves unworthy to be loved, so that their loss or disappointment becomes also a threat of producing separation from those who are loved, even though no actual separation has occurred. Loss of money, failure to reach an important life objective, criticism from a person specially valued or feared, illness, etc., operate in this way as precipitating stresses.

One finds that if the individual in his early development has been thwarted in satisfying basic oral and love needs, he has strong feelings of hostility to those who have so thwarted him in his desire for gratification and love. However, with a formidable superego (conscience) the individual cannot discharge this hostility directly—it is instead redirected against the individual himself and against his introjected images of the person who is both loved and hated. Thus the self reproaches are, ultimately, in the depressed individual, a merciless criticism of the primary love object (mother or father) who first failed him. This hostility is often concealed behind a façade of passivity and submissiveness. Actually, the basic personality of the depressed patient is that of a self-centred (narcissistic) egotistical individual, extremely sensitive to criticism, disapproval or rejection, and with strongly ambivalent (mixed love and hate) feelings to everyone and everything. A life experience which is traumatic then sets all the old grievances in motion.

The following case illustrates many features of a depressed reaction.

A 49 year old male, 5 months in Canada as a displaced person, complained of depression, weeping spells, fatigue, chronic dyspepsia, inability to concentrate, poor sleep, loss of appetite and thoughts of suicide. Since arriving in Canada, he was unable to get employment because of his age, language problems and lack of demand for his type of training (whisky distiller). However, he managed hopefully on agency assistance, supplemented by his daughter's earnings, until he learned that his wife had an inoperable carcinoma of the stomach. In anticipating her death he developed the acutely depressed reaction. Physical examination revealed no pertinent abnormalities. Neurological was normal. The content of thought dealt mainly with ruminations over his impending loss, together with cries of desolation and self-pity, weeping storms and interjections of suicidal urges. He felt inferior, lacked confidence, was self-critical, avoided meeting people or venturing into the street.

Because of the practical limitations of out-patient care, and the severity of the reaction, a course of electroshock treatments was initiated. Six treatments were given with temporary improvement at first, then the improvement was consolidated after 6 more electroshock treatments. The major symptoms then subsided and he was treated subsequently with vitamins, divided doses of somnol* and psychotherapeutic interviews.

The background history indicated that his father was narrow, sadistic, strict, religiously fanatic. There was always a deep fear and hatred of his father. His mother was kinder, protecting him partly from his father's wrath, but he blamed her for not protecting him more, and for having so little to give him as the younger children were added to her burden. As a child he was timid, easily frightened, and terrified of the dark, of storms, of dogs and persistently of his father. He resented his older brother who was more successful and had privileges of the firstborn, but he hated violently his father, for his cruelty and rejection, also for his harshness towards the patient's mother. At 15 he had to leave his father's home to make his own way in the world. He was desolate, homesick, unhappy, but he could only pay his mother visits that were secret from his father. He always felt depressed and weighted whenever his father was near. In his teens, after several failures because of his querulous timidity and nervous dread of the boss, he was taught his trade by his older brother. With girls and socially, he was shy and reserved. His sexual life began late, and was filled with anxiety and associated tormenting guilt, because of his religious morality. His courtship lasted 8 years. He could not decide to marry because of his own anxiety, his mother's objections and his concern about the dowry. He finally married at the age of 28. Difficulties began at once. He had ejaculo præcox, and found his wife to be frigid and unresponsive to his excessive needs for affection. Further conflict developed with his mother-in-law: in this he felt that he had no support from his wife. He felt desolate then; he had incurred his mother's hostility by his marriage, and now his wife's love and sexual rejection. Within a month of his marriage he became deeply depressed and remained so for about 10 months. During this period he attempted suicide by slashing his throat. He only began to improve when he began psychotherapeutic interviews and separated his wife from her family and took up residence in another city. During his illness, his only child, a daughter, was born. Following his recovery he got employment and was more successful, but he remained very resentful to his wife for her inability to satisfy his love and sexual needs. He was jealous of the child behind a façade of paternal solicitude. His wife, at one point, became ill and he frankly wished her death, as he was at that time, engaged in a sexual relationship with a war widow, whom he hoped to be free to marry. His daughter was aware of this liaison, his wife was not. During the war years, he was for a time in a slave labour battalion, then was in a D.P. camp from 1946 until his immigration to Canada in April, 1949.

Concealed beneath the idealized protestations about his wife's benign and wonderful character, and the enormity of his loss in her impending death, was a welter of hostilities and resentments to her, which began to emerge in the psychotherapeutic interviews. As this material was ventilated under permissive guidance, his guilt and hostility to himself began to diminish. When his wife actually died, there was no further grief, as the mourning reaction had already been worked through in the period anticipating her death. However his search for a new object became intense, as his dependency needs had to be gratified. He complained bitterly at first of his daughter's coldness to his desperate pleas for affection—he wanted her to take his wife's (mother's) place. He reported, with anxiety, dreams in which he gave his daughter an engagement ring as a suitor, another in which sexual intercourse with her took place (factually they share the same room for sleeping quarters). His demands for help from other sources were also excessive at first, from the therapist for daily interviews, from Social Services, from the Agency. As the therapeutic relationship strengthened, and he improved, these

* Product of Messrs. Frank W. Horner Ltd., Montreal.

frantic demands diminished. At present he is working part time, his depression is lifted even though his wife's death is only 6 weeks ago, and he is generally much improved. His psychotherapeutic interviews are still essential in sustaining him and will be necessary for some time. His satisfactory transference to the therapist diminishes his excessive demands on others, particularly his daughter, with whom serious conflicts are thus being averted. He is being helped to an adjustment in the midst of a major upheaval in his life. Efforts are now directed to further diminish his guilt and to increase his ego strength so that he can become more self sustaining in the future.

In review, this case presents the typical features of a depression, and the personality of the patient and the psychological mechanisms illustrated are fairly characteristic. The patient is very narcissistic, extremely dependent on external supplies of affection and love in order to maintain equilibrium. There is the hostility and ambivalence to the parental figures. There were repeated minor depressions in early life, a major adult depression reactive to sexual frustration, and then the development of the present illness as an exaggerated anticipatory grief reaction. The actual death and the increasing emergence of hostility to her and to earlier figures in his life is coincident with steady improvement.

TREATMENT

A plan of therapy must be based on a clear evaluation of all the factors involved, including the clarification of the stress factors, and the dynamic delineation of the patient's personality structure. Therapy is directed first at the alleviation of symptoms and the protection from self-destructive drives, and secondly, by helping to restore more normal relationships, the distorted personality forces (super-ego-ego).

The first decision concerns the immediate environment of the patient. It must be determined whether therapy can be proceeded with in the home setting, or whether removal to a relative, a hospital or nursing home is necessary to reduce conflicts and tensions, or to anticipate suicidal drives. Should the patient be treated at home, an assessment of the charged relationships in the home is at once necessary, in order to instruct the family what to do, what to avoid. This is no simple task, as it often turns out that each one has his own beliefs about behaviour causation in general and this illness in particular. Tactful firmness is necessary right from the start. An unhealthy setting which cannot be modified necessitates removal to a general hospital or a suitable nursing home. Commitment is necessary in the presence of serious suicidal threats or when the patient because of agitation or other reasons, requires mental hospital care. Sometimes, with special supervision, even a critical illness period can be managed without commitment.

Drug therapy.—Many agents are used symptomatically in depressions. Tonics, vitamins, insulin subcoma and nutritional adjuncts may be useful in specific cases. Generally, however, these measures are of no value. Appetite, weakness, weight loss do not respond until the primary mood disturbance is treated. Hormone therapy is used in depression at the climacteric or involutional period. The dosage is much larger than when used for menopausal states without the additional depression. Hormone therapy fails to restore the libido in the presence of persistent depression. The problem is one of psychological imbalance rather than of glandular imbalance. Sedation is used to alleviate tension and agitation, and to make sleep possible. Satisfactory oral sedation is provided by the rapid acting barbiturates given in divided doses. Sodium amytal gr. 1 or gr. 2, t.i.d. is helpful. Somnol in divided doses is also useful. Parenteral sedation, by the intramuscular or intravenous route serves multiple purposes. In addition to giving some relief and relaxation to the patient, it permits the therapist to reduce the inhibited state and allows catharsis and ventilation to take place. Intravenous sodium amytal in experienced hands is especially useful. As a matter of fact, it is recommended as a therapeutic test, and a prognostic guide to the efficacy of electroshock therapy. Satisfactory relaxation and an elevation of mood are good signs. It should be pointed out that sedatives should be under the supervision of a responsible person and not given to the depressed patient directly or in quantity. The temptation to suicide is always to be remembered in the management of the case.

Stimulants, at whatever level they act on the nervous system, are disappointing. Benzedrine or dexedrine compounds help reduce fatigue occasionally, but seem otherwise valueless in the patient who is really depressed. Desoxy-ephedrine hydrochloride (methedrine pervitin) has recently been described as an intravenous agent to combat tension and de-

pression, and aid catharsis. It is promising and merits further investigation. A combination of sedatives and stimulants (sodium amytal plus benzedrine) has been useful at times when agitation and depression are both present. Benzebar* is after the same order.

Psychotherapy.—The depressed patient presents special problems. In a deeply depressed state, too early analysis of the disturbing factors, and confrontation and hurried interpretation can be extremely disturbing, and, in unwary hands, may provoke a suicidal attempt.

The main need at first is to establish rapport, and provide constant reassurance of recovery, the feeling of sympathetic interest and protection from the therapist, and gentle probing to bring to light the basic hostilities and to reduce guilt. The therapist may need temporarily to function passively as a substitute for the individual who has been lost to the patient. Once rapport is strong enough, the primary problem is to help the patient redirect his hostility from himself (in the depressed state) to external objects once more. In further therapy, the superego is gradually modified in its function, and the ego strengthened so that future stress can be better tolerated.

In a deeply depressed state, the patient can be so regressed psychologically as to be inaccessible to the doctor. Then it is, that other measures are useful to reduce barriers blocking the psychotherapeutic relationship.

Electroshock therapy.—Electroshock therapy can rapidly terminate the depressed state, effectively and safely in a high proportion of cases. Since the introduction of shock therapies, numberless patients have been saved from commitments, suicide or a lengthy period of misery. At first only used in mental hospitals, in recent years ambulatory E.S.T. has been successfully introduced at this hospital and others. Strauss and Macphail,[2] Impastato,[3] Zeifert,[4] Feldman[5] and others have reported on various aspects of the ambulatory treatment of both inpatients and outpatients at the general hospital level. Fetterman[6] lists the advantages of ambulatory E.S.T. as saving in time, in expense, in hospital beds, avoiding the stigma of institutionalization, and helping towards more rapid recovery. The disadvantages are the increased responsibility placed upon the family, and the increased opportunity for suicidal acts. The careful selection of patients is imperative. The severity of the reaction, the duration of the illness, the age and physical status of the patient are important factors. The excessive caution regarding physical contraindications to treatment which existed soon after the introduction of convulsive therapies, has, to some extent been allayed.[7] Each patient has a careful physical examination, with x-rays of the spine and E.C.G. when indicated. The usual complication is a post-treatment memory defect which clears spontaneously after a few months. In our series, of a total of 1,669 treatments given, there were, in 3 cases compression fractures of a lumbar vertebra, without severe symptoms, and, in 1 case a fracture of the scapula. Nowinger and Huddelson[8] reported that the cortical changes, revealed by E.E.G. changes after E.S.T. are reversible. Huston and Strother[9] concluded that—"E.S.T. does not produce any significant impairment of mental efficiency after an interval of 6 months". It may be stated that in experienced hands and with careful precautions, the dangers are minimal.

Diagnosis	*No. receiving treatment*	*Recovered*
Primary depression (Involutional)	145	113 (78%)
Schizophrenic reactions	11	3 (27%)
Manic	7	5 (71%)
Paranoid reactions	6	3 (50%)
Psychoneurotic reactions	9	2 (22%)
Undiagnosed	5	2 (40%)

Ambulatory E.S.T. has been carried out at this hospital during the past 30 months. A total of 183 patients have received treatment, and a total of 1,669 treatments have been administered. Of this group, 125 were female, 58 male. By diagnosis, 145 were primary depressions or involutional melancholias (79% of total), 11 schizophrenic, 7 manic, 6 paranoid reactions, 9 anxiety states and 5 undiagnosed. The average number of treatments given per series was 7. Some patients received repeated series, either for relapse or new attacks of illness: 18 patients (10%) relapsed. A recent follow-up inquiry has been carried out, and enables an evaluation of the results to be made. The overall picture is found to be encouraging: 134 patients (73% of total) reported themselves completely recovered or much improved; 18 patients relapsed, either getting further E.S.T. or other treatment (commitment, etc.),

* Product of Messrs. Smith, Kline & French, Philadelphia.

22 patients reported no improvement; 9 others discontinued therapy or were unavailable for follow up. Of these diagnosed depressions, 113 (78%) reported recovery. Manic showed a good response also.

SUMMARY

1. The signs and symptoms of depressions have been outlined, and the diagnostic implications discussed.

2. Precipitating factors, pathogenesis, and the interplay between environmental stress and the vulnerable personality have been described, and clarified by the presentation of a case.

3. Management of the depressed patient has been considered under the headings of manipulation of the environment, drug therapy, psychotherapy and electroshock therapy.

4. The results of ambulatory electroshock at this hospital are presented.

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METABOLIC DISINTEGRATIONS*

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TWO approaches to the problems of human metabolism have contributed largely—possibly predominantly—to our understanding of this subject. The use of the respiratory exchange and of nitrogen balance as indices of the success or failure of the organism to maintain a state of metabolic integration, and the observation of disease states where metabolic disturbances are the main feature, are both classical methods. Less interest has been shown in those *transitory* derangements of metabolism which occur frequently during the course of an illness but which are of only minor importance. Yet the very fact that such disturbances are not clinically very important suggests that they differ from the normal in degree rather than in kind and are therefore worthy of particular attention. During and after the war my colleagues and I had some opportunities to observe many different examples of this type of metabolic disturbance. It seemed appropriate to present an account of our work and to show how our findings did not always coincide with classical metabolic concepts.

Alterations in metabolism, whether of rate or direction, must result ultimately, with minor exceptions, from changes affecting enzyme systems of the body. These changes may arise within the organism or may be caused by some change in the environment. Research in physiology and biochemistry today is concerned increasingly with the mechanisms whereby the organism relates the speed of specific enzymic reactions to its continually changing environment. If these reactions were not co-ordinated and integrated, cellular existence would cease. Many of the sequences of intermediary metabolism are now known in detail, but the problem of how these multitudinous enzyme systems are integratively controlled is today only just being posed. This changing emphasis from the analysis of individual enzyme systems to the problems of their integration one with another stimulates renewed interest in the classical work on the metabolism of the intact organism. Many of the theoretical concepts with which we approach such problems today are derived from these early experiments, and it is fitting that we should re-examine them in the light of our present knowledge of intermediary metabolism and nutrition.

The heat production of intact animals is a good index of the intensity of the metabolic processes, but the direct measurement of it demands an elaborate apparatus which is impracticable for clinical work. When Benedict and Joslin[1] showed that under standard basal conditions it was possible to obtain good agreement between direct determination of the heat production and heat production calculated from the amount of oxygen consumed over a known period, it became possible to use the indirect method in routine clinical studies. The adoption of Rubner's concept[2] that the heat production per unit surface area was constant for a given species enabled comparisons of heat productions of different individuals to be made

* The Banting Memorial Lecture, University of Toronto, February 14, 1949.

and eventually led to the construction of standard tables of reference by Boothby and Sandiford.[3] Intensity of metabolic processes is now expressed as the "basal metabolic rate" which is the difference between the heat production measured indirectly and that taken as the standard for an individual of the same age and sex, expressed as a percentage of the standard rate. This symbol or index of metabolic activity, however, involves an assumption which is not universally true. This assumption is that the mass of active metabolic material relative to a unit of surface area does not alter significantly whatever the state of nutrition of the individual may be. Such an assumption is unwarranted when the subject being studied has suffered a severe weight loss.[4] In such cases the fall in basal metabolic rate is due to a fall in the amount of active material per unit surface area and is not due to a decrease in the intensity of the metabolic processes. Heat production (or oxygen consumption) per unit body weight in these cases does not change significantly from the normal.

Another concept which is very widely held today derives from the pioneer work of Magnus-Levy.[5] He showed that heat production was high in exophthalmic goitre and low in myxœdema. Subsequent workers have demonstrated the central rôle which the thyroid plays in the control of the metabolic rate. The tendency has been to assume that any variation from normal must be related to abnormal thyroid activity. This assumption is by no means valid, even where there is no abnormality in the weight/surface ratio.

Benedict, Miles, Roth and Smith[6] showed in normal subjects and Joslin[7] in diabetics that reduction in food intake led to a reduction in the conventional basal metabolic rate. Such findings need not imply any reaction by the organism other than an inability to produce heat from food that is not there. In the Benedict experiments healthy young adults were placed on low food intakes for three weeks, which resulted in a weight loss of 10.5%. The basal metabolic rate, however, fell by 19%. In Joslin's subjects who had lost .35% of their body weight the fall in the basal metabolic rate was only 22%. Joslin calculated that in the Benedict series a 1% fall in body weight brought about a fall of 1.8% in the basal metabolic rate, but only 0.63% in the diabetics. If Benedict's results be interpreted, as he interpreted them, as indicating a protective reaction of the organism to poor food intake, then why should this protective reaction be proportionally less in Joslin's diabetics? If the fall in basal metabolic rate in Joslin's series is in fact due to a change in the ratio of body weight to surface area, then Joslin's subjects, far from demonstrating a reduction in the intensity of heat production, in fact had either a normal rate of oxidation in their tissues or an increased one. We expected to find in our starvation cases a fall in the rate of oxygen consumption whether calculated in calories per square metre of body surface or per kilogram body weight. In fact the calories per square metre showed a percentage fall correlated with the percentage fall in body weight, while the calories per kilogram body weight were not significantly different from the normal.[8] Starvation in our subjects had not altered the rate of oxygen utilization by the tissues.

When re-feeding began, the rate of oxygen utilization rose, but in spite of this the body temperature did not increase above the initial subnormal level until some days later. The change in the rate of oxygen consumption was rapid and could be reversed equally rapidly if the food intake was lowered. This type of response to re-feeding was similar to that described by Coleman and Du Bois[9, 10] in convalescent typhoid fever patients, but the magnitude of the response was less marked in their patients. This increased oxygen consumption persisted for about one week and then gradually fell. When carbon dioxide outputs were measured simultaneously with oxygen consumption it was observed that the rate of production showed no significant change from that found in the earlier phase. The respiratory quotient thus approached or exceeded unity. One supposes that oxygen-rich metabolites were then being converted into oxygen-poor ones. The fall in oxygen consumption from the atmosphere was presumably due to the formation of fat; in fact, subcutaneous fat was being deposited rapidly.[8] If carbon dioxide excretion is an index of oxidative activity, subjects in this phase appear to continue the high rate of oxygen utilization seen in the first phase, while simultaneously producing fat. We have no evidence which throws light on the reason for this change in the metabolic picture. Takahira[11]

gave data which show that after a 12-day fast the respiratory quotient exceeded unity after the second day of re-feeding. He too noted an increase in oxygen consumption during this period, but it must be pointed out that on the 11th day of re-feeding the oxygen consumption exceeded that observed in the control period by only 16%. Carbon dioxide production on this day exceeded the control level by 23%. His results differ from ours in their magnitude, which is to be expected, because of the short period of food deprivation in his experiments. An increase in oxidative reactions and simultaneous rapid formation are not incompatible provided the energy content of the diet is adequate.

Studies of the respiratory exchange can sometimes reveal a breakdown in a specific enzyme system. Simonart[12] measured the oxygen consumption and carbon dioxide output in a group of inmates in a Belgian civil prison during the German occupation. The food intake during the period of observation varied between 1,550 and 1,850 calories per day. On this diet he found in some subjects that the R.Q. remained persistently above unity. He found in these individuals that blood pyruvate was markedly elevated. As there was a marked clinical improvement when thiamin was added to the diet, he attributed the metabolic disturbance to a failure of the aerobic oxidation of pyruvate to carbon dioxide, through the tricarboxylic acid cycle. Thiamin deficiency was rare in Holland in 1945 and as far as we are aware, unknown in Germany in 1946. In our Dutch studies we saw no clear indication of a thiamin deficiency. We observed a few individuals with R.Q.'s in excess of unity on diets containing around 1,500 calories per day and in them a reduced alkali reserve, but as we had not determined the blood pyruvate or lactic level, the cause of these disturbances was not established. The importance of thiamin, riboflavin and niacin in intracellular oxidative catalysis is well known from experimental work, but there is a paucity of data from human cases of avitaminosis on the metabolic disturbances produced under such conditions.

Nitrogen balance studies in the classical papers were in large part concerned with the factors involved in securing nitrogenous equilibrium. Less attention was paid to the question of the rate at which protein could be synthesized. But out of this work there grew the concept of the protein sparing action of non-protein foodstuffs which Cathcart[13] showed was almost entirely attributable to carbohydrate. The problem of maximal protein sparing by non-protein dietary components resolves itself into two questions: (1) on how low a protein intake can the human subject maintain nitrogenous equilibrium? (2) how much dietary protein above this level can be utilized for tissue regeneration? Information on the first point is plentiful in the literature. Siven[14] and later Chittenden[15] found that it was possible to reduce the daily nitrogen input and output to about 0.1 gm. N/Kg./day. In our Dutch series we found that equilibrium was attained at a higher level—0.17 gm. N/Kg./day. The probable explanation of this discrepancy is that in their experiments the ratio of non-protein to protein calories in the diet was about 15 (Siven) and 11 (Chittenden), whereas in ours it did not exceed 5. One would expect the answer to the second question to be contained in the first. Provided sufficient calories are available in non-protein foods to cover the energy expenditure of the body, the greater part of any protein ingested in excess of the basal requirements should be available for tissue regeneration. This presupposes, of course, that the amino-acid composition and the vitamin content of the diet be adequate; conditions which should be largely in force with high animal protein intake and vitamin B-complex supplementation. On such diets one would expect emaciated individuals to conserve vast quantities of nitrogen in the attempt to replace lost tissue. We found, however, that in the Dutch series the percentage of input nitrogen retained was only infrequently greater than one-third. This was not due to faulty absorption from the intestine; it was not due to a badly-planned diet, as supplementation with raw liver, methionine, or replacing the standard diets by "fresh-food" diets of similar protein, fat and carbohydrate content caused no improvement. The subjects, being weak, easily fatigued and content to remain almost immobile in bed during the greater part of the day, should have had a marked surplus of calorie intake over output, as many of the diets exceeded a caloric value of 3,000, and the basal metabolic rates were low. None the less, we were tentatively forced to conclude that the

caloric requirements of these subjects for maximum nitrogen retention were not being adequately met. When nitrogen retention was examined in relation to the nitrogen and calorie equivalents of the diets, it was found that at the higher levels this was unrelated to the former, but almost directly related to the latter. Unfortunately we have no balance studies with very high caloric intakes, but for a few patients records of intake were kept after the end of the balance period. Suddenly increased rates of weight gain were noticeable in these subjects. They occurred at a time when the diets, freely selected by the patients, contained between five and six thousand calories per day. Unless there is some limit to the rate at which the body is able to synthesize new protein, one is forced to conclude that an enormous energy expenditure must be incurred in the side-reactions which supply energy for the process of protein synthesis itself. It has already been pointed out that oxygen consumption rose greatly in the early phase of re-feeding and that later the tissue oxidations indicated by carbon dioxide production were apparently still proceeding at a high rate.

The highest sustained positive nitrogen balance for a limited period (6 days) of which we are aware is a case (F.R.) reported by Mulholland *et al.*[16] It represents the conservation of 142 gm. of protein per day. To this must be added the amount of protein synthesized to replace that destroyed by tissue "wear and tear". Assuming that 0.1 gm. N./Kg./day represented protein so synthesized, Mulholland's subject would therefore have to produce an additional 31.5 gm. protein. A daily protein production of 173.5 gm. would thus be required to satisfy the positive nitrogen balance and minimal "wear and tear". Is this near the upper limit of protein synthesis in man? No certain answer to this can be given, but if the findings of Robscheit-Robbins *et al.*[17] in plasmapherized dogs can be applied to man on a body weight basis the potential daily protein production of a protein depleted subject weighing 50 kg. would be around 220 gm. per day, excluding that required for "wear and tear" replacement. As their dogs could store only 50% of the fed protein, the daily protein intake required to produce the synthesis of at least 220 gm. protein per day would be 373 gm. The diet would have to contain an adequate amount of non-protein foodstuff to prevent the fed protein being used as a source of energy. Mulholland *et al.* obtained 66.5% conservation when the non-protein calorie ratio was 4.7 and we obtained our highest percentage retentions on a ratio between 5.4 and 5.5. Taking a ratio of 5, the diet which might be required to yield a protein conservation of 220 gm. a day, would contain 1,530 protein and 7,650 non-protein calories, or a total calorie intake of 9,180 calories. Although intakes of this magnitude have been recorded, no details of their effect on protein metabolism are available. It would appear probable that even if an upper limit to protein synthesis exists, it is unlikely that it would be reached except under a most unusual combination of circumstances.

The primary factor in limiting the rate of protein synthesis may not, of course, be a dietary one at all. Attention recently has been focussed on two groups of hormones which may influence the balance of protein destruction and regeneration in the body. Browne and his collaborators in Montreal have noted a correlation between adrenal cortical activity and nitrogen metabolism.[18] Normal subjects after injury frequently excrete large amounts of nitrogen in excess of that ingested. This "catabolic reaction" is accompanied by a marked rise in the level of urinary glycogenic corticoid excretion, and is not apparently inhibited by increased food intake. Other individuals, usually elderly persons or those who have undergone a long period of undernutrition or chronic illness, do not pass through this catabolic phase following acute injury, and do not show evidence of increased adrenal cortex activity. Browne's suggestion that the adrenal cortex, by means of a hormone which stimulates protein destruction, is responsible for the above-mentioned catabolic phase is in line with present concepts of the relation of the gland to the process of gluconeogenesis, but has not yet been confirmed by direct experiment. Kochakian[19, 20, 21] has drawn attention to another group of hormones which may directly influence the balance of protein synthesis and degradation, namely the androgens. These hormones may be produced either by the adrenal cortex or the testis, and, if injected into normal or chronically undernourished individuals, cause a marked decrease in the level of urinary nitrogen excretion without affecting energy metabolism. The possibility that our famine cases had excessive adrenal cortex activity or diminished

production of androgens is very real. Unfortunately the only evidence we have on these points is indirect. The observation of low-normal lymphocyte counts in the blood and the not infrequent occurrence of hyperglycæmia with insulin resistance may support the view that cortical hormone secretion was increased. The frequency of sexual regression in the same subjects was so high as to leave little doubt that there was diminished activity on the part of the gonads. Sterility in both sexes was quite common. Testicular atrophy with loss of libido, and amenorrhœa were found in all severely emaciated persons. Loss of body hair was also common in both sexes.

The study of clinical conditions in which hepatic function is disturbed affords many opportunities for metabolic investigation. It is well known that a dietary deficiency of choline or its precursors, one of which is methionine, can result in the accumulation of fat in the liver. This deposition may be so excessive as to interfere with other hepatic functions such as the elimination of bile pigments, the production of glucose and storage of glycogen. It may even cause a mechanical obstruction to the flow of blood through the liver and thus lead to necrosis. Increased fat deposition may occur in carbon tetrachloride poisoning. In this condition the drug may bring about a choline deficiency,[22] or it may interfere with the mechanisms of lipid phosphorylation which are known to be concerned in the turnover of fats by the liver.[23] The study of a case of carbon tetrachloride poisoning in man[24, 25] showed that methionine administered during the phase of hepatic enlargement caused a rapid return of the organ to its normal size. Presumably fat had left the liver. Twenty-four hours later the liver again enlarged. Methionine again caused the liver to shrink and to remain in its normal state. It is possible that methionine had acted through the phosphorylating mechanisms and had merely repaired a deficit of choline. In more severe cases of carbon tetrachloride poisoning, hepatic enlargement may be accompanied by a marked ketosis. When methionine is administered to such cases the hepatic enlargement is rapidly diminished, but the ketosis is made much more severe. Some cases did not show ketosis but when methionine was given it appeared. Glucose with or without methionine had no effect on the ketosis, but when insulin was added to the solution of methionine and glucose the ketosis rapidly disappeared. Thus if we regard methionine merely as a choline precursor, it exerts the expected lipotrophic action, and in severe cases it accelerates the production of ketone bodies to a level higher than their rate of utilization. Insulin appears to increase the rate of utilization of these ketone bodies, presumably effecting their conversion into glucose and thence into fat.[22] This interpretation is consistent with the work of Stetten and Boxer[26] and Stetten and Klein,[27] who showed that insulin accelerates the synthesis of fat from glucose or from molecules smaller than glucose. The fat so formed would, in the presence of adequate quantities of lipotrophic material (methionine), be rapidly transferred from the liver cells.

This explanation of the effects of methionine in carbon tetrachloride poisoning is, however, not complete. We found in the case we reported in 1944 that sulphur metabolism was disturbed. In normal subjects the infusion of 10 gm. of methionine over a period of 1 to 2 hours is followed by the appearance in the urine within 24 hours of the greater part of the methionine sulphur. This sulphur, however, appears as 70% oxidized (sulphate) sulphur and 30% unoxidized (neutral) sulphur. In our case only 33% of the methionine sulphur excreted was oxidized, the remainder appearing as neutral sulphur. We have given reasons for suggesting that this neutral sulphur may be accounted for as an amino-acid (not methionine). We noted that during the 12 hours after administration of methionine when the liver was retracting rapidly, there was no rise in the rate of urinary sulphur excretion. As there was no evidence of disturbed renal function, we may presume that the sulphur-containing fraction of methionine was retained in the liver for a longer period than usual, and eventually excreted largely as an unoxidized compound—possibly an amino-acid.

This finding is of interest in view of Miller and Whipple's finding[28] that massive hepatic necrosis after chloroform anæsthesia in protein-depleted dogs could be averted by the administration of methionine or of choline with cysteine, but not by the administration of choline or cysteine alone. Massive hepatic necrosis was found in one fatal case of carbon tetrachloride poisoning which we observed, and

it is likely that the metabolic disturbances in this condition are similar to those found in chloroform poisoning. If this be true, methionine may have two separate hepatic effects in carbon tetrachloride poisoning; one which is purely lipotropic and due to the rôle which methionine plays as a choline precursor, and a second which depends upon the properties of the sulphur-containing amino-acid.

The commonest hepatic diseases during the war years were infective hepatitis and its closely related disease, homologous serum jaundice. The metabolic disturbances in these diseases resembled in many ways those found in carbon tetrachloride poisoning. In the milder forms hepatic enlargement was often relatively small, but in more severe types a swollen tense liver was detected especially during the first week after the onset of symptoms. Retraction of the liver occurred when methionine was given. The urinary sulphur then showed a high proportion of unoxidized material. In very severe cases when retraction of the liver had taken place methionine was of no value. In such cases autopsies revealed extensive or complete necrosis. Between the moderate type with enlargement of the liver and the fatal type with hepatic necrosis there was every gradation. Ketosis was common in this intermediate group. As in carbon tetrachloride poisoning it was combated by the combination of methionine, glucose and insulin. In contrast to diabetic ketosis, recovery from the comatose state was slow, taking in some cases as long as 36 hours after the institution of treatment, although ketone bodies had disappeared from the urine within a few hours after treatment began.

Infective hepatitis, however, displays metabolic disturbances other than those which might be associated directly with alterations in fat metabolism. During the prodromal and acute phases the subject is in negative nitrogen balance. In most cases there is an abrupt transition from a lethargic state with anorexia to alertness with marked increase in appetite especially for protein foodstuffs. When these are provided the nitrogen balance becomes positive with a continuation of nitrogen excretion at the preceding level. When appetite returns but the food intake is still restricted, the administration of methionine does not bring about positive nitrogen balance. If food intake is raised before appetite returns the nitrogen balance does not become positive.[29]

In carbon tetrachloride poisoning and in infective hepatitis, the severity of the clinical effects might be interpreted in terms of the breakdown of different enzyme systems. The early increase in liver size might indicate an increase in fat content due to choline deficiency. Following this, the enzyme systems requiring organic sulphur might be affected causing the appearance of large amounts of unoxidized sulphur in the urine. Later in more severe cases the appearance of ketosis would indicate a failure to dispose of the ketone bodies either by oxidation or in the synthesis of fat. This explanation of the metabolic upsets in these conditions is obviously somewhat specious and tentative. It leaves out of account the rôles which the endocrine glands may play in the breakdown process. We may ask: why does the islet tissue not respond sufficiently to prevent the development of ketosis in severe hepatitis and in carbon tetrachloride poisoning; and does the adrenal cortex play any part in the production of the negative nitrogen balance in both these clinical conditions? And again, what part does the anterior pituitary play during the hepatic upset? The rapid resolution of the abnormal metabolic pattern in even moderate cases of infective hepatitis has impressed us. On one day the patient is dull and lethargic, with anorexia and nausea and in negative nitrogen balance; on the next he is an alert and hungry man clamouring for a steak and eating it with relish. He passes immediately into positive nitrogen balance which may on the first day of increased food intake reach a level of 12 to 16 gm. N. What is the key change which effects such a dramatic return to a fully co-ordinated and normal metabolic state?

We have drawn attention already to the increase in basal oxygen production which occurs immediately after re-feeding is begun in starvation subjects and have related the rate of increase to the level of calorie intake. We have noted also the high rate of protein destruction which occurs on such diets. In the later phase the oxygen consumption fell but carbon dioxide production and nitrogen output in the urine remained at or close to the levels found in the first phase. We concluded that the fall in oxygen consumption in the second phase was to be explained by a rapid formation of fat from

oxygen rich metabolites. It would be reasonable to conclude that the high rate of oxygen consumption on the recovery phases indicated an adequate production of insulin. Moreover as Stetten and Boxer[26] have shown that fatty acid production is reduced to 5% of normal in diabetics and Best[22] stated that the prompt synthesis of fatty acids is one of the major actions of insulin, the rapid fat formation in the second phase also suggested a high rate of insulin production.

Investigations carried out within 48 hours after admission showed that carbohydrate metabolism was not then normal. The subjects fell into two distinct groups. In the first the resting blood sugar levels lay between 75 and 105 mgm. %, while in the second group they lay between 125 and 160 mgm. %. Insulin sensitivity was increased in the first group and markedly decreased in the second. After ingestion of 50 gm. of glucose the subjects in the first group gave peak blood glucose levels between 230 and 250 mgm. at 60 to 90 minutes, but those in the second group gave peak levels between 160 and 200 mgm. at the same time. After three hours the blood glucose level had fallen to within 15 mgm. of the resting level. At no time did any subject present any sign of ketosis.

The subjects in the first group were obviously examples of "hunger diabetes".[30] They may be presumed to have had a reduced insulin production but no other endocrine disturbance. Repetition of the various tests on the 7th hospital day when each subject had been on an increased food intake for at least four days gave normal responses. The second group presented a more complex problem. The hyperglycæmia and increased resistance to insulin suggested an increase in the production of diabetogenic hormone by the anterior pituitary. On the other hand, when these subjects were placed on a high carbohydrate and protein diet they showed a marked increase in oxygen consumption. They did not develop a ketosis, nor did the insulin sensitivity, resting hyperglycæmia and flattened glucose tolerance curve change until after 3 or 4 days on the diet. It must be concluded therefore that insulin production in these subjects was adequate for glucose utilization in the tissues. Moreover, they all showed a high rate of urinary nitrogen excretion. The carbon residues of the amino-acids were presumably transformed into glucose and perhaps into fat under the influence of insulin. The complete restoration of the normal metabolic pattern by the end of the 7th hospital day when the diet was high in carbohydrate and protein and subcutaneous fat was being deposited rapidly indicated that the islet tissue had suffered no damage because of the increased production of diabetogenic principle. Haist, Campbell, Ham and Best[31] have shown that insulin can protect islet tissue from damage by the diabetogenic principle. The flattened glucose tolerance curve might be attributed to the rapid storage of glycogen in the muscles,[32, 33] but it might equally well be due to increased glucose utilization in the peripheral tissues under the influence of insulin. It would appear that these subjects had increased production of insulin and diabetogenic principle at rates which enabled their effects to be balanced at a raised resting blood glucose level. It is not known whether this state had existed for a long time before admission, but apparently a state of hyperglycæmia without ketosis and with increased insulin resistance can exist for some years without permanent damage to the islet tissue. In 1946, Dr. A. de Vet and I examined a woman, aged 41, who showed hypothermia, hyperglycæmia, insulin resistance, absence of ketosis and a flattened sugar tolerance curve. These persisted until 1948 when it was noted that the resting glucose level and the glucose tolerance curve had returned to normal. The resistance to insulin had disappeared, but hypothermia persisted.

This case is of interest for another reason. The clinical findings suggested to three independent observers that a lesion of the hypothalamic area was the most probable cause of her condition. These opinions were expressed before the metabolic disturbance was detected. Davison and Selby[34] described a case with identical metabolic changes and clinical findings almost identical with those in this case. At autopsy they found a localized lesion of the hypothalamus and no evidence of any histological change in the anterior pituitary. Yet they produced unmistakable evidence of early acromegalic changes in the skeleton. If we accept the work of the school of the Cori's[35, 36] that the hexokinase system is inhibited by anterior pituitary extracts and that this inhibition is released by insulin, it is conceivable that the production of diabetogenic principle by the anterior pituitary may be mediated by some neural

mechanism involving the hypothalamus. It would, however, be necessary to ascribe an inhibitory function to this mechanism.

Before the question of hypothalamic control of carbohydrate metabolism can be considered, it will be necessary to clarify the problem of anterior pituitary control. The association of acromegaly with hyperglycæmia and decreased insulin-sensitivity states is well-known, but although there is much experimental evidence to suggest the identity of the growth hormone with the diabetogenic principle of the pituitary, this identity has not yet been proved. Hyperglycæmia and increased resistance to insulin are, however, found in many cases of Cushing's syndrome. The mechanisms in this condition must be different from those involved in the disturbed metabolism of acromegalics.

A metabolic inco-ordination may arise at many levels in the metabolic pattern. It may be due to a blocking of a single enzyme system or of one component of that system. On the other hand, it may arise from a brain lesion which produces an effect only through the intermediary of one or more endocrine tissues. The determination of the primary cause does not, however, constitute a solution of the problems of inco-ordination which arise from that cause. The discovery of insulin did not solve the problems of diabetes; rather it led to an appreciation of their complexities. Best followed a trail which led to the discovery of lipotrophic factors and the mechanisms of lipoid phosphorylation. In another direction the trail led Houssay and Young to the discovery of the rôle of the anterior pituitary. Another trail has opened out as Long and Browne explore the significance of the adrenal cortex in the complex relationship between protein and carbohydrate metabolism. But in spite of the efforts of countless workers over a quarter of a century we are still uncertain of the full extent of the insulin effect on metabolic processes.

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TRANSURETHRAL URETEROLITHOTOMY*

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IT is generally accepted that the majority of ureteral calculi will either pass spontaneously or be treated successfully without too much effort. However, there exists a group of approximately 20% of cases, that will require more elaborate therapy. Some of these will be treated readily by open operation, others will respond to some form of accepted endoscopic manipulation, but there remains a small category of patients with stones impacted in the intravesical portion of the ureter, which resist all forms of transurethral manipulation. It is this latter group of cases which we are concerned with in this presentation.

The desirability of endoscopic removal of ureteral calculi, situated in the terminal intramural portion of the ureter, has taxed the ingenuity of the urologist, in devising mechanical devices for the extraction of stones. The methods employed are legion, and the group includes ureteral dilatation with bougies, the

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multiple catheter and loop catheter methods, the various stone baskets, the metal corkscrew, and the method of enlarging the ureteral orifice with the cystoscopic scissors, the Colling's knife or fulgurating electrode. Coppridge and his group have recently described a series of cases, of direct manipulation of low ureteral stones, *per urethram,* in which an alligator forceps was passed alongside the cystoscope, and grasped calculi within the ureteral orifice.[1] Lowsley has had good results with the forceps bearing his name, in extracting calculi about to enter the bladder.[2]

All of these procedures have met with varied success in the hands of different operators. Since so many devices have been advanced for the extraction of low ureteral calculi, it becomes obvious that no single method has completely solved the problem. We have used all the forms of treatment mentioned above, but in our experience, the old established method of ureteral dilatation with bougies has been most effective. We have had moderate success with the wire basket, and the metal corkscrew, but have not been impressed with the other procedures noted above.

We first used the method of transurethral ureterolithotomy to be described, in January, 1949, when the following problem presented itself. A male patient, age 45, was admitted to the Jewish General Hospital, with left ureteral colic. Investigation revealed an impacted stone situated in the intramural portion of ureter, at a distance of 1.5 cm. from the ureteral orifice, with considerable hydroureter and hydronephrosis, as shown by intravenous urography (Fig. 2). There was marked œdema of the ureteral orifice, and the catheter could not be passed beyond the site of obstruction. Repeated attempts were made to extract the stone, under spinal anæsthesia, without success, as no instrument including the bougie, wire basket or metal corkscrew

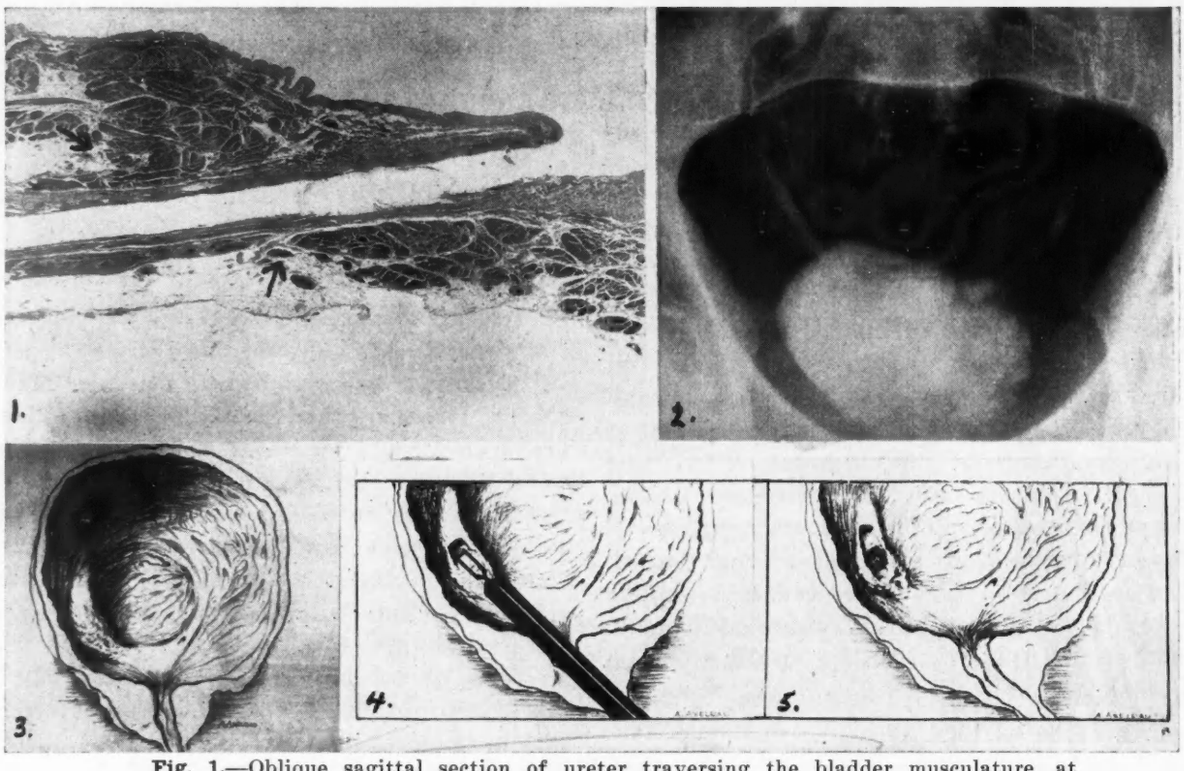

Fig. 1.—Oblique sagittal section of ureter traversing the bladder musculature, at routine autopsy. Note the longitudinal muscle fibres of the ureter extending through the interlacing bladder muscle fibres. The length of intramural portion of ureter varied from 1.5 to 2 cm., and this distance was considered the margin of safety in operating. The two arrows indicate the danger points in resecting the orifice, at the point of entrance of ureter into bladder. **Fig. 2.**—Intravenous pyelogram in the first case, showing a large low impacted ureteral calculus, with dilatation of the ureter, and irregularity of the vesical contour, due to extensive bullous œdema. **Fig. 3.**—Artist's drawing at cystoscopy, of an œdematous, bulging ureteral orifice, resulting from an impacted stone in the intramural portion of the right ureter. **Fig. 4.**—First cut with the resectoscope loop, starting above the area of bulging, approximately 1 cm. from the ureteral orifice. **Fig. 5.**—Stone is situated in its bed, after the roof of the intravesical portion of ureter has been removed, and about to be snared with the resectoscope loop. In most cases the resection includes the free lip of the ureteral orifice, which however was not removed in this case.

could bypass the impacted stone. At this point an attempt was made to enlarge the orifice with the cystoscopic scissors, but as so often happens, bleeding obscured the field of vision before sufficient enlargement could be obtained. On the following day, since the patient had considerable pain and tenderness in the loin, with fever, nausea and vomiting, with a mass in the loin, immediate operative intervention was indicated. In the past, in a situation of this sort, a ureterotomy or cystotomy was performed. Since this patient was acutely ill, it was decided to attempt the removal of stone by resecting the ureteral orifice, with the resectoscope loop. Accordingly, under spinal anæsthesia, the Stern-MacCarthy resectoscope was introduced, the intravesical portion of ureter was laid open, and the stone removed with the loop. The procedure took approximately 10 minutes, was technically not difficult, and bleeding was minimal, being readily controlled with the coagulating current. A self-retaining catheter was inserted and left in place. The postoperative course was uneventful.

The procedure proved so satisfactory, that it was decided to employ this method in similar future cases. We feel certain that many urologists have resected the ureteral orifice in similar circumstances, but in a perusal of the literature, we have been unable to find mention of this method. It is for this reason that we considered it of interest to discuss the subject. Since then, we have attempted the procedure in 15 additional cases. Successes were obtained in 13 cases, with 2 failures.

Following our initial case, in which this method was used with good result, our attention was naturally directed toward an accurate knowledge of the anatomy of the intramural portion of the ureter, and in particular an estimation of the absolute limits of safety, in performing resection of the distal extremity of ureter for the extraction of stone. Accordingly, in collaboration with the Department of Pathology, sections were cut at routine autopsy, of ureters entering the bladder (Fig. 1). It was found that the intramural portion of ureter measured 1.5 to 2 cm. in length, and this distance from the point of entrance of the ureter into the bladder musculature, up to the free margin of the ureteral orifice, was considered the margin of safety in this procedure.

Before attempting the procedure, certain criteria must be fulfilled. Firstly, the stone must be present in the terminal intramural portion of the ureter. Second, it must be so impacted that all other forms of treatment are unsuccessful, due to the inability to bypass the calculus with any of the instruments, such as the bougie, basket or corkscrew. Thirdly, the cystoscopic view must reveal a definite bulge, just above the œdematous ureteral orifice. This bulge of course, is caused by the stone and the dilated ureter above it. Lastly, an x-ray should reveal an opaque stone in the terminal portion of ureter. This is most reassuring to the operator. Up to the present, we have not attempted the procedure in non-opaque impacted ureteral calculi.

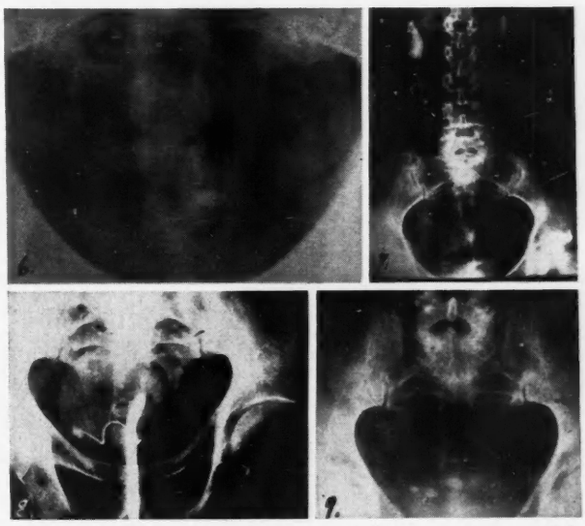

Fig. 6.—The largest stone in this series, which measured 1.4 x 0.4 cm., and successfully removed by resecting the ureteral orifice. **Fig. 7.**—Postoperative intravenous pyelogram, taken two months after resection of the right ureteral orifice, showing no evidence of obstruction in the upper urinary tract. This is representative of the follow-up pyelograms in these cases. **Fig. 8.**—A large impacted ureteral calculus, in the intramural portion of ureter, which was successfully removed, by resection of the orifice. **Fig. 9.**—Two large ureteral stones, the lower of which was impacted in the intramural portion, which were removed in succession, by endoscopic resection of the right ureteral orifice.

The operation is fairly simple, and it is carried out under low spinal anæsthesia (Figs. 3, 4 and 5). The resectoscope is introduced, and directed toward the affected ureteral orifice. The roof of the intramural portion of the ureter, and the corresponding portion of the floor of the bladder surrounding the stone are then resected, proceeding with great caution and employing shallow bites, until the stone is brought into view. Following this, the lateral walls surrounding the stone are then excised to enlarge the orifice, and the rectoscope loop is

then employed to snare the stone into the bladder. It is important to maintain proper visualization, at all times, by coagulating the cut surface of the orifice immediately. Bleeding at operation has, however, not been troublesome, although we have had one serious case of postoperative hæmorrhage, which will be discussed under complications. In one of our cases, after resecting the orifice a moderately large calculus was found to be impacted, and could not be moved from its bed, with the resectoscope loop. However, it was successfully dislodged with the metal corkscrew, which was readily inserted beyond the stone, and drew it into the bladder (Fig. 6). In 2 of our female cases, the calculus was readily palpated *per vaginam*. It was possible, by exerting pressure upward in the vagina, to accentuate the mound in the bladder, thereby facilitating the operative procedure. It is our policy to insert a self-retaining catheter postoperatively, and patients are given penicillin and streptomycin as a prophylactic measure. Following discharge from hospital, these patients are asked to return for intravenous urography, 6 weeks after operation, in order to determine whether or not stricture has occurred at the site of operation. Six of these patients have had cystoscopic examination in periods varying from 6 weeks to 4 months, postoperatively.

The possible complications to be considered in this procedure are (1) perforation of the bladder, with urinary extravasation, (2) stricture at the site of operation, (3) hæmorrhage and (4) infection. In none of our cases did the first 2 possible difficulties arise, namely rupture of the bladder, or stricture of the ureteral orifice. As to the morbidity following operation, it was noted that a mild febrile reaction, up to 100° occurred in most cases, but rapidly subsided within 24 hours. In two cases, the temperature rose to 103°, with chills, but returned to normal within 48 hours. One of these followed removal of the retention catheter, and the temperature returned to normal upon reinsertion of the urethral catheter. In the second case, the marked febrile reaction was attributed to probable œdema about the ureteral orifice, with temporary impairment of drainage and upper tract infection.

Bleeding at operation was minimal in all cases, and easily controlled with the coagulating current. We had one postoperative hæmorrhage occurring 36 hours after operation, despite the fact that there was no undue bleeding during the procedure. Unfortunately the patient developed bladder clot retention, and was returned to the operating room, where a large amount of blood clot was removed, transurethrally. Two days later he developed chills, with high fever up to 104°, and pain in the left loin, the side of operation. A ureteral catheter was inserted up to the left renal pelvis, and a large quantity of infected old bloody urine was aspirated, from which *B. coli* was cultured. The temperature returned to normal within 48 hours, following which the ureteral catheter was removed. Two days later, the patient began to bleed, the temperature rose, with pain and tenderness in the left loin. An intravenous pyelogram showed a non-functioning left kidney, and the renal shadow appeared quite large. Examination of the left loin revealed a large tender mass. A repeat cystoscopy showed a large organizing blood clot plugging the left ureteral orifice, which could not be removed, with all our manipulations. The patient was acutely ill, with high fever, rapid pulse rate, and the impression at this time was that an acute pyelonephritis, with marked infected hydronephrosis, was present on the affected side. Operation was considered mandatory, and a left nephrectomy was performed. The kidney showed multiple cortical abscesses, in addition to an acute hæmorrhagic pyelonephritis. The ureter was filled with old organizing blood clot, and culture from the renal pelvis, again showed *B. coli*. It is interesting to note that this patient was the only one in our series that developed serious complications, which ultimately resulted in nephrectomy.

We have attempted this procedure on 16 patients with low ureteral calculi. There were 13 successes, in which the stone was removed transurethrally, and the patient made an uneventful recovery. In 2 of our early cases, the stones were not removed in this manner, because they proved to be beyond the limits of safety. In retrospect, we realized that they should not have been attempted endoscopically, and subsequent ureterolithotomy was performed from above. The other failure has already been described. The stone was readily removed, but the subsequent course proved devastating, as we have already noted.

The size of the calculi removed was over 1 cm. in diameter, in over 50% of cases, the largest

being 1.4 x 0.6 cm. (Fig. 8), the smallest, 0.4 x 0.4 cm. The average postoperative stay in hospital, in the successful cases was 4 days. This does not include the complicated case described above.

In our follow-up of these cases, we were naturally anxious to see what the ureteral orifice looked like, several weeks after operation, and to ascertain whether or not, stricture and hydronephrosis had developed. Accordingly, we performed intravenous pyelograms on these patients 6 weeks to 3 months after operation, and cystoscopy on 6 patients, 6 weeks to 4 months postoperatively. We were gratified to find that the resected ureteral orifice, while slightly enlarged and somewhat distorted, was normal in all other respects. No evidence of ureteral stricture, hydroureter, or hydronephrosis was noted in any of the cases treated in this manner (Fig. 7). In addition, a cystogram performed on 3 patients showed no reflux up the ureter. The majority of patients showed pyuria for approximately 2 weeks. In two of the patients, in spite of medication, pyuria persisted for 2 months, and finally cleared.

SUMMARY

1. A suggested form of transurethral ureterolithotomy, using the resectoscope, for impacted stones in the intramural portion of ureter has been presented.

2. The procedure in no way replaces the well established endoscopic forms of therapy, but is offered as an added aid to our armentarium in dealing with low ureteral calculi.

3. In our experience, the procedure is technically not difficult, and the complications are minimal. We urge however that care ~~be taken~~ to establish certain criteria, discussed above, before the procedure is attempted.

4. We have found it of practical value in the acutely ill patient, with infected hydronephrosis, for whom open operation would prove hazardous.

We wish to express our indebtedness to Dr. M. A. Simon, for his co-operation in the anatomical studies of the lower ureter; Dr. A. Axelrad for the drawings of the procedure, and Dr. M. Siminovitch for the photographic studies.

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WHAT THE GENERAL PRACTITIONER AND THE INDUSTRIAL PHYSICIAN SHOULD KNOW REGARDING THE PROBLEMS OF RETIREMENT*

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THE proportion of our older people, 65 years of age and over, has risen from 4% of the population in 1900 to 10% in 1950. Science and Medicine have progressed more rapidly since 1900 than in all preceding time. New discoveries and processes have been accepted and utilized in an orderly manner: the problem of an older people still lacks understanding through dearth of research and education.

Whereas the financial security of this older group is at present receiving consideration by a special committee of our Federal Government, there has been little leadership given on any level to the biologic, mental, and social processes of this aging group. Sporadic attempts have been made by various educational or community groups toward a solution. It is a difficult task, for no precedent has been established or co-ordinated research carried forward. Much popular and serious writing on the situation has appeared in the past five years, generally dealing with an already old people, outlining cures for existing ills, while too little has been done in the preventive field where, through education in the score of years prior to the designated age of 65, many of the maladjustments can be avoided, and the usefulness of older age utilized to the benefit of both the individual and society.

The Second World War caused industry to use men and women in the older years, with varying physical handicaps, to keep up production. That this older group did faithful work, with less absenteeism, and less tendency to accident is a recorded fact, but, the advent of peace time activity has tended to discard their services, until today it is difficult for men and women 45 years of age and over to obtain employment.

Newer concepts by psychologists and social workers maintain that the needs of older people differ little from those of youth or middle age, and that there is a vast productive waste in the

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non-employment of the aged. The individual is in an unhappy situation while society, so far, has been unable to offer a solution.

Three years ago, the University of Michigan, through the Institute for Human Adjustment, began and continues to expand its classes in "Aging and Maturity" in order to discover techniques for the management of this problem; truly a pioneer effort on a new frontier, whose results are setting a pattern for all work in this field. Senator Desmond, in the State of New York, has a fact-finding commission on this subject, the tentative conclusions being published in the book, "Birthdays Don't Count". The Federal Security Agency of the United States Government have set up a "Working Committee on the Aging" to correlate the various plans and methods used in various agencies throughout the country and to give not only leadership but assistance in the understanding of the adjustments required in this ever increasing proportion of the population.

Any physician who has been concerned with the health of industrial workers, or who practises in an urban centre, realizes the uncertainties and unhappiness of this aging group. He is aware of the necessity for research and is anxious and willing to do his part in arriving at a solution.

Over the last thirty years I have been in general medical practice in Windsor and have also been employed as medical director of the engine plant of General Motors Corporation on a part-time basis throughout this period. The hobby of industrial physician thirty years ago, as the result of this last World War, became almost a vocation, due to increased employment and the advance in medical care of workers. For the past two winters I have had the pleasure of conducting classes in the education of working men of General Motors and their wives, 45 years of age and over, in the problems ahead of them in their later years.

Our medical records, over the years, of men employed originally at age 20 to 25, show the results of aging in an active industry. Today I see these men growing older, changing from healthy youth to an aging people with financial, health, and social obstacles. Some of these men have retired as a result of crippling illness, others fear retirement on a company pension scheme while the great majority even at 65, are physically able and desirous of carrying on at work. Let me illustrate the problem of industrial physician and general practitioner, by three actual experiences.

J.S., aged 42, was medically examined for a position with this company. He was required for rather heavy work in the cylinder block department. The man had previously been employed for seventeen years in a foundry; at age 38 he left the foundry and opened a hardware store. After a struggle with this for four years, the business failed. He was forced to seek work again. Originally a robust young man, he had by now gained 100 pounds in weight, smoked heavily, drank beer as so many foundry men do, with the result that at his General Motors examination he weighed 220 pounds, 5′ 5″ in height, with a blood pressure of 180/120. Looking ahead 20 years to the time this man would be 65 years of age, it was considered he would be a risk to himself and his employer, making it necessary to refuse him work.

Mrs. M. was a widow aged 72, whose husband, at one time was a prosperous business man, until the depression took the business. At his death his widow was dependent on $40.00 per month, old age allowance, forced to live, cook, and sleep in one room, lonesome, friendless, and distraught. She came to my office with a complaint of indigestion arising from malnutrition and undernutrition. This condition was remedied to a certain extent, but she came back frequently with various complaints, until I realized that, for a 3 o'clock appointment, she would arrive at 1.30, enjoying talking to my nurse and other patients. It was apparently to be my duty to imagine various other symptoms for her, so that she must be in my office weekly. The visit to the doctor's office was her only diversion of the week, a substitute for the movies. At the moment there are three widows in like circumstances, who use my waiting room one afternoon each week as a club room.

Finally, Mr. X, former president of a large, successful company, with adequate finances, was retired at age 65. His family are all alive, but living in Great Britain, the United States, and Western Canada. They have families and responsibilities of their own. His wife is alive and well, interested in many philanthropies. The retired president, leaving active business, with no preparation for older living, has developed complaints which an hour's chat disperses, relieving his loneliness, and finally resulting in his doing active community work in the city. The two years' change-over period, from competitive business, through sitting idle, to a new outlet in community work, almost took his physical and mental machine into an irreversible breakdown.

These experiences raise the problems older people must meet, that their needs and satisfactions out of life are not far removed from the needs of earlier years.

The following questions arise: Is this aging process becoming more distressing, more evident today than formerly, and is there not some prophylaxis to the distress of growing old?

The increase in numbers of older people 65 years of age and over, rising from 4% in 1900 to almost 10% in 1950, can be attributed, in great measure, to advances in medical science. The principal factors are the prevention of infectious diseases, the control of infection by

the antibiotics, the safeness of surgery in older people, and now a more alert public to the research in the field of arthritis and other crippling maladies.

While medicine, then, is greatly responsible for longevity, is it making men at age 65 more mentally fit and physically active than heretofore? There has, so far, been great effort given to prevention and treatment of disease, can we not afford to give more time to maintenance of health?

The distress of our senior population, both male and female, has been increased in the recent twenty years through a changed pattern of living. We have, in your time and mine, left an agricultural era of the nineteenth and early twentieth century, for the modern industrial economy, with its need for mechanization and more rapid mode of living. This industrial activity has brought men and their families to the cities, until now over 55% of the population of Canada is living in urban communities. In the rural areas when the farmer and his wife become too old to work the place, the son with his wife take over the farm. The old folk move to one part of the house, taking with them their life-long possessions, doing chores, the mending, living privately as before, but happily with work, friends, and a feeling of usefulness.

Before contrasting this with city living may we consider the loss of the family unit which has arisen along with the so-called progressive industrial years. Children, today, are individuals, wishing to follow their own ideas and not content to carry on with the affairs of their fathers. There is such increased mobility and ease of movement that the young people accept opportunities in any country or at any distance from the homestead. They marry, raise families, in cities with a dearth of housing, and find their own difficulties in the mere mechanics of living, perhaps laying aside a little for their own future. The close tie with the others in the family disappears.

Aged parents, forced to live with their sons or daughters in cities, must, in many instances move varying distances, leave friends, live in one room, without their possessions about them, with little opportunity to find work, and experience a high cost of living. Soon they feel in the road, unwanted, and lonely from loss of companionship. They, so often, finish up their years in a most unhappy state, reflected also in the lives of their children.

To recapitulate, then, we have an increased life span, a population shift, a loss of family cohesion, making for a confused distress in 10% of our population. Industry is just beginning to recognize this situation, while the community and society are tardy in setting up proper educational and recreational facilities.

May I review a preventive method which we have employed in an experiment at the 600 man plant of General Motors in Windsor.* It is the belief of our personnel and medical departments that if proper education in physical, mental, economic, and social needs be given to working men and their wives, at the age of 45 years and up,—newer techniques in living can be understood and practised during the productive years remaining, so that when retirement from the daily work arrives, there is, ahead, a new life, as interesting, as active, and as satisfying as the early years.

Classes held during the past two winters, attracted an average of 80 employees and their wives. The various problems of later living were outlined and discussed by invited University professors or well-qualified lay speakers. A word of explanation as to why the wives are included in this educational program.

(*a*) Should the man retire from active work, for any reason, the wife does not cease her daily routine but has the added annoyance of the man of the house hindering rather than helping in the daily home operation.

(*b*) Men and wives seem diffident about discussing the problems of later maturity on a sane basis. The position of growing older, perhaps dependent, is not talked about, whereas, in a class room, with free discussion of the eventualities of later life, the subject is introduced. There will be criticism, based on their own personal situation, nevertheless, the subject of future living is brought into the open.

(*c*) Frequently the man dies, leaving a widow to face life in an altogether changed environment. Adjustment can only come through understanding, while complete maladjustment through ignorance of later situations is not only unpleasant but unnecessary.

(*d*) At 45 years of age, with children leaving home, or about to do so, the parents are still in

* This pilot experiment does not represent a policy of General Motors Corporation.

a position to knit the group together, so that pride and love of home remains a living reality, where all members make for an integrated unit.

The following needs were included in our series of lectures:

1. *Financial security.*—To-day 45% of our population at age 65 and over, are independent, living either on earnings alone or supplemented by pension or use of savings. The remaining 55% are dependent on private or public charities. Some new skill developed in the last two decades, can be the means of providing a revenue in addition to any pension, so that independent living can be maintained.

Could I illustrate this by the story of one of our union stewards, who gave this talk at one of our classes. This man raises canaries, for show purposes. He brought the birds to the class, demonstrated their qualities, explained the feeding and rearing of the singing varieties, and ended by saying, "If I ever lose my job or retire, I can make a handsome living raising canaries, selling bird seed and cages".

Another man, born in Poland, described his raising bees, and with his still accented speech, told a fascinating story of his future independence. He had learned the whole bee-keeping art, through government periodicals and trial and error.

2. *Physical and mental health.*—A knowledge of biologic aging is necessary. There is a rapid decline of certain physical faculties with a persistence or often increasing development of the spiritual, emotional, and mental abilities. Our examination of sick people has alerted us to better diagnosis of disease. We can tell the patient what ails him, but can we also tell him how much workable machinery is left, how to utilize this remaining health to the best advantage? If remedial defects are discovered at age 45, through periodic physical examination, many of the degenerative diseases can be aborted. Men and women, at this age, are receptive to preventive medicine, and will truly endeavour to correct existing faults.

Our general physical examination should leave time enough to listen to the whole life story of accomplishments and discouragements. Here we will see the human being stripped down—at last, he has found a listener who understands. A great deal of psychosomatic complaints can be laid to the physicians's lack of time to hear the story. At the moment the experiment is being carried on in several industries in London, Ontario, where a padre is on the personnel staff, one who saw active war service and is skilled in understanding. His work is praised by men and management. We, in our practices, can learn and take time to give this valuable service to our middle-aged patients.

3. *Living arrangements.*—Where, with whom, and how to live out our later years? This is not only for our patients but also for ourselves. Early thought in the still productive period of life can be not only a great adventure but also have a very practical application. The need for satisfactory housing facilities for older people is critical, for housing is not only shelter but also a living arrangement. Older people do not desire to give up their homes, the retention of which can create an expense often beyond the reduced income to provide.

The great anxiety of older people, when they arrive at advanced years, is the fear of lack of care in critical illness. This fear may be the prime reason the older person will sacrifice his independence, his comrades, and often all his resources, to enter a home.

The foreman of our Tool Room, aged 49, has six children, three married, and living away from home, and three at home, ages 13-11-6. His wife came from a small town, where the family had a few acres about the house, the man, city bred. Two years ago, they sold their home in the city, and moved to a small village a half hour's drive from Windsor. Their entire mode of life has changed. Although housing facilities are quite up to the city standard, the social life is different. The wife is interested in church and institute work, while the husband can scarcely wait to get home to work with the different projects on his six acre estate.

It is the physician's duty to know the advantages and disadvantages of country living as compared with village or city conditions. Whether it is best to live alone, go with the children, or take the married son or daughter to live with them. All the various modes of life in the later years can be obtained from just listening to the stories of older patients. I do not believe the final answer has been given to the housing problem of the newly retired or the very old, the well or the sick aged, the husband and wife, or one of them going on alone.

(4) *Activity.* (5) *Companionship.* (6) *Pride.* —All of these needs of life, whether in youth or middle age, carry on into late maturity and are essential to health and happiness of the very old.

Some occupation, previously thought out, and for which preparation has been made, where useful work, if necessary for financial assistance, or in some Community service where contact is made with others of the same age, and more especially with people of a younger group, can be carried out. This useful activity plus companionship will bring with it the pride of work, the feeling of being wanted, which makes for both mental and physical health.

Mention might here be made, of hobbies; those pure diversions or time-killing pursuits. They are only of value to any individual if they produce the three factors just mentioned. It is a rare individual indeed, who can work away at a stamp collection for instance, if he cannot show the results of his hobby to other collectors, talk over with them the fine points of this pastime, and receive the praise or congratulations for their efforts.

7. *Religion.*—The spiritual and emotional mental functions remain at a high level of activity from 45 years onward. Advancing years, with loss of friends or family, makes religion a real need, not only for solace and comfort, but as a final rock on which to stand.

After retirement—what? Several methods have been proposed for making the period of unadjustment, immediately following retirement, less distressing. It is generally believed that some contact, however slight, with the former work place is most desirable, and makes possible a speedy readjustment. At the Vauxhall plant of General Motors in England, there exists a pension scheme whereby working men must leave their employment at age 65. At once, they become eligible for membership in the Retired Employees Club. Meetings of this group are held weekly in the winter months and monthly during the summer. All problems arising out of their retired state, whether it be housing, financial, or otherwise, are brought before a select group known as "The Brains Trust". As this brains trust includes two past directors of the company, the problems receive excellent handling, and the advice given the troubled enquirer is of sound value.

To conclude, then, we as physicians in caring for our aging population, whether we work directly with the employees in industry or as private patients, require to know, not only the diseases which affect the aged, but also, the various requirements of the older group for a happy, zestful, useful later life and be prepared to listen and counsel constructively.

THE INFLUENCE OF THE PERTURBATIONS OF CHILDHOOD LIFE UPON THE OCCURRENCE OF APPENDECTOMY

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IT has long been known that the organism must adapt itself to its environment. In psychiatric literature, the mechanism by which this adaption to exogenous and endogenous stimuli occurs is usually said to consist of the cerebrospinal and autonomic nervous systems.[1] The endocrines appear to be left out or assigned a minor rôle in psychiatric thinking about the adaption mechanism.

In 1944 Hans Selye[2] suggested that certain common and grave diseases of child and adult life were the result of an endocrinal mechanism involved in the organism's adaption to stressful situations, He called this mechanism the General Adaption Syndrome. Because our later schizophrenics all show childhood growth disturbances,[3] because of Selye's later paper on the effect of prolonged hypercorticoidism upon the brain of the rat,[4] and because of the frequency with which physical growth lag is accompanied by lag in intellectual growth as measured by Stanford Binet tests,[5] we have added "Brain" to the syndrome.

More than three years' experience with the recording of childhood-growth measurements, combined according to time with known potential stress situations and illnesses upon the Wetzel grid,[6, 7, 8] has convinced us that Selye's general adaption syndrome is the only explanation of part of what we see, which very briefly is as follows.

Changes occur in the auxodrome (the curve of combined height-weight vs. age curve on the right chart of the Wetzel grid) related to the onset of known emotional stress situations, but

unrelated often to the onset of even certain later fatal diseases, or to change in dietary intake. Indeed, we have many records of fatal diseases where no change occurred in the auxodrome whilst the child was still in school, even though advanced disease existed. This finding is in part confirmed by the fact that Leeson, McHenry and Mosley[9] report that more than half of the children in a North Toronto School suffered change in nutritional state and developmental lead or lag with no change in dietary pattern or onset of disease, and by Fried and Mayer's[10] observation upon closely observed institutionalized children that lag in growth could only be abolished when emotional stresses were removed.

All diseases of the general adaption syndrome almost invariably are preceded by developmental lag or lead (acceleration or retardation from the expected of the combined height-weight factor on the Wetzel grid), if the measurings are closely enough spaced together in time. The length of time this lag precedes the onset of the adaption disease usually depends upon the chronicity of the disease. Rheumatic fever, for instance, is usually preceded by several years during which lag exists whereas an acute appendicitis is usually preceded by only months of lag. Again, the onset of the lag is related to the onset of usually easily ascertained stress situations and not to changed dietary pattern or ascertainable disease.

Amongst the diseases which Selye suggested might be due to the hypermineralocorticoidism arising out of stresses was appendicitis and its corollary, appendectomy. Because appendectomy is a definite event confirmed by an abdominal scar, it was decided that a study should be undertaken to determine its relationship to stressful life situations and to the general adaption syndrome. It is not unusual for children to report after several weeks' absence from school that they have had rheumatic fever, or a rheumatic heart condition where little evidence exists of such. Tonsillectomy is so frequently encountered that in many cases some doubt must exist after Kaiser's careful study[11] of its efficacy as a preventive of the ills of childhood, and of its need. Rheumatic heart disease and nephritis are fortunately uncommon.

It was determined that events which might lead to emotional stresses rather than opinions about parental attitudes such as rejection, etc., should be selected as the potential stress situations. Where adverse attitudes were very marked they were included separately. It was well realized in doing this that the attitudes and success with which a family faced up to an event which might prove disastrous was the important thing about the event, and that a parental attitude interpreted by the child as an adverse one might far outweigh in importance any perturbation which ordinarily might happen. However, it was determined to use events rather than opinions of attitudes. The date of an event such as parental death, is a remembered one, whereas the date at which a child becomes aware of a hostile parental or teacher attitude may be extremely indefinite.

In selecting appendicitis we are mindful of the fact that its etiology is regarded as bacterial; but we are also aware of Litman and Bosma's[12] study of the effect of preceding developmental lag or lead upon the onset and severity of poliomyelitis, also an infection, in the 1946 Minnesota epidemic, where a high proportion of children (over 90%, according to a personal communication) apparently required poor growth records in order to suffer the disease, whereas their siblings with normal growth records usually escaped the disease. Further, we are cognizant of Mechem Fuller's studies[13, 14] on Affectivity and Growth.

The children selected for controls are all from the public and separate schools of Saskatoon and appear in our current file on February 28, 1950. The appendectomies studied were all in children of the above who had been subjected by that date to the operation. The information was gleaned from their medical records. For many years we have recorded the marital status of the parents, their socio-economic status, and any apparently significant social data. There is necessarily a time lag in the collection of such data, but the time lag is equal for the controls and the appendectomized. Unfortunately, it is too seldom realized by parents that factors disturbing the emotional calm of the home have a real bearing upon school achievement. Consequently, social data in this small city are collected in bits, but after several years they are probably more accurate than they would be in a larger centre. Further, at the present time we are seeing the children of parents who were themselves scholars when we began our work 21 years ago.

In addition to the above controls are added the proportions of Grade VII students from a former study of the past year as an additional control. Considering that the average age of Grade VII is considerably above the average age of all students in school it would be expected that the perturbations of life would have occurred more frequently by that age, and that in this group parental enlistment would be less frequent. However, the two groups show striking similarity.

There were 6,517 children, of whom 3,340 were males. There were 263 who had had appendectomy, and of these 3 had had appendectomy concomitant with herniotomy. Twenty-two appendectomized children were known to have had "chronic" appendicitis.

In Table I we give a summary of our findings. Unfortunately it was impossible for our small staff to ascertain the ages of the controls. However, the percentages of boys and girls per grade follow. Our children begin kindergarten the year they are five, and if they pass each year they should complete Grade VIII and end school at fourteen. The sex-grade incidence was:

TABLE I.

	Boys	*Girls*	*Both*
	percentage	*percentage*	*percentage*
Kindergarten	4.8	4.7	9.6
Grade I	8.3	6.8	15.1
Grade II	7.2	6.8	14.0
Grade III	6.6	5.4	12.1
Grade IV	6.2	5.0	11.1
Grade V	4.6	5.8	10.4
Grade VI	5.2	5.5	10.7
Grade VII	5.3	5.2	10.5
Grade VIII	5.1	5.8	10.9
	51.2	48.7	

In this census 355 special class children were omitted.

It was found that there was a steady increase in the proportions of the children who suffered appendectomy up to the age of eight and then a steady decline. It is striking that boys suffer appendectomy in their preschool and early adolescent periods in larger number than girls, the latter however, undergo appendectomy in larger number during the latent period, (6 to 10 years), so that there was no significant difference *in toto* as far as sex was concerned.

It was felt that the date of appendectomy might be of interest. This follows:

TABLE II.

1934	1 case	1940	7 cases	1946	35 cases
1935	1 case	1941	9 cases	1947	44 cases
1936	1 case	1942	11 cases	1948	43 cases
1937	2 cases	1943	18 cases	1949	21 cases
1938	3 cases	1944	24 cases	1950	5 cases (to February 28, 1950)
1939	4 cases	1945	34 cases		

Total: 263 cases.

Thus there has been a very sharp increase both at the time of heightened war activity and again in 1945 when the Saskatchewan Hospital Service Plan for "free" hospitalization came into being in July, 1945. A reference to the economic status of the children appendectomized shows that, contrary to most diseases, appendectomy is overwhelmingly (two-thirds) amongst the upper socio-economic groups, a situation quite contrary to our previous findings with goitre[16, 17], but not contrary to the implications inherent in Stern's[18] finding. Thus the provision of "free" appendectomy (patients are notorious in regarding the surgeon's account as the one to be paid, if at all, last) may in some measure be responsible for the rapid rise after 1944, rather than the stress of adjustment to a returned veteran father.

Another factor that should be mentioned is that yearly since 1946 we have suffered a spring and fall epidemic of gastroenteritis. Curiously this was most severe in 1949 and thus most easily diagnosed. Perhaps that year our local surgical staffs were more reluctant to perform appendectomy because of the prevalence of the epidemic. The differential diagnosis between mild cases of gastroenteritis and an apparently mild appendicitis is not often worth the risk of error, and appendectomy was rightly performed in 1946 onwards; 1950, from its early record, promises to be another 1948 in the higher incidence of the operation.

A third factor, that should be mentioned because it preceded some cases, was inoculation. Immunizations may be stresses to some children, particularly children who show some growth disturbance from stress already present as the result of a previous perturbation or adverse attitude, or from endogenous stress. Additional stress increases their endocrine imbalance, as shown by increased growth disturbance, continuing for as long as several years following immunizations. McCloskey's[21] recent

paper has shown how the stress of inoculation "pushed" some children into suffering poliomyelitis.

Most noticeable of all was the relationship between tonsillectomy and appendectomy; 25.3% of our controls have suffered tonsillectomy to date. But amongst the appendectomized children 34% suffered tonsillectomy previous to appendectomy, and 27% of the remaining non-tonsillectomized children have undergone tonsillectomy to date, with most of them having some years of school yet remaining in which to undergo tonsillectomy. More than 50% in constrast to the 25.3% of the controls, have had a tonsillectomy, with the probability that before they leave school the proportion will be nearly 70%.

The age at which tonsillectomy was performed is significant: 723 of the 1,403 tonsillectomized children suffered tonsillectomy before they were six years of age. The proportion of tonsillectomy amongst the appendectomized was similar. Were it not for the existence of so many known stress situations during the preschool period it would almost appear that tonsillectomy predisposed the child to later appendectomy. In addition to the 723 tonsillectomized children there were 8, not included, who underwent adenoidectomy.

We had no opportunity in these cases for personality studies. However because since 1935 every child measured had pelvic width also measured, and because personality and type of build may be related, we studied the distribution

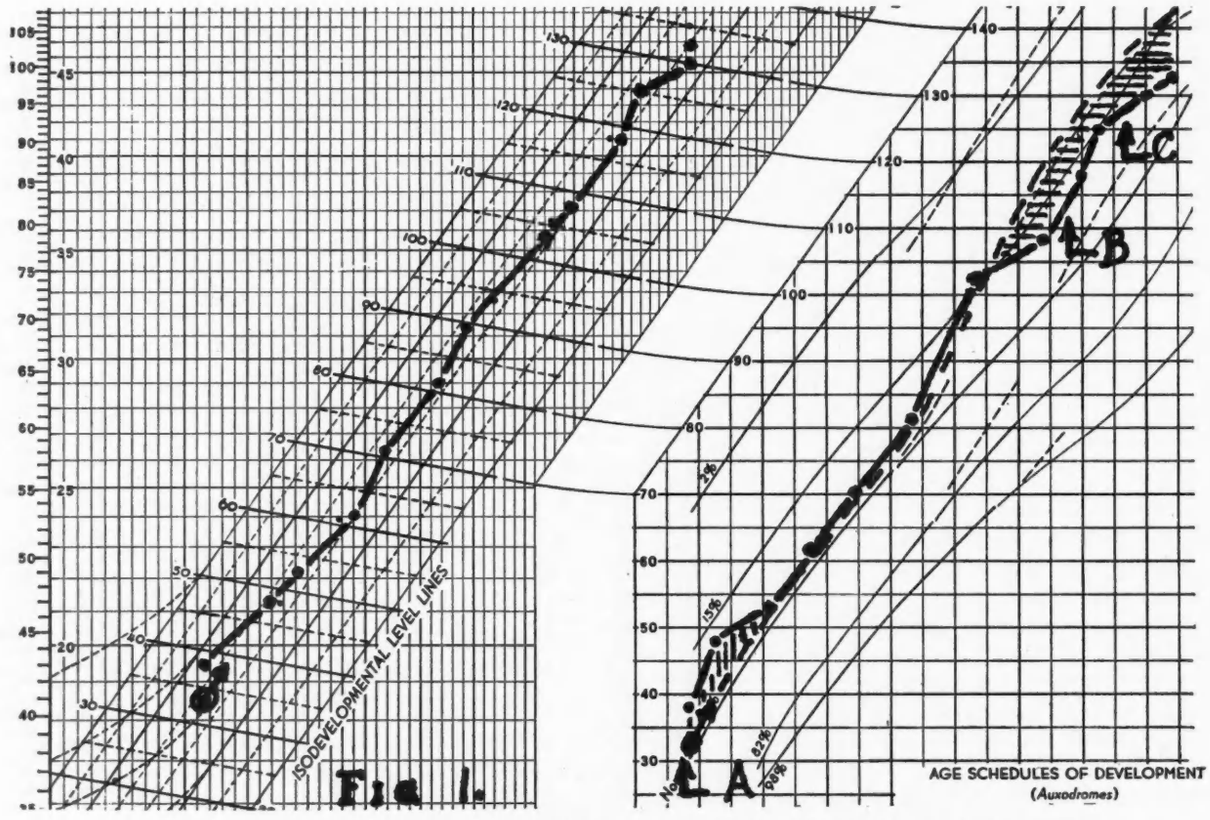

Fig. 1.—On the left chart of the Wetzel grid weight is plotted against height. The plottings fall in channels. Those of heavier for height children fall in the upper left channels, whilst those of lighter for height children in the lower right channels. Across the channels at such an angle that all children on the line have equal basal metabolic requirements are placed numbered "development lines", the point reached by combined height and weight.

On the right chart this level of the height-weight factor, the development level, is plotted against age. Superimposed are typical curves of various sized children that this curve should follow. The child's record is thus compared with itself, and any deviations from the expected are easily seen.

We use a weight-width chart to determine the expected channel and development level by plotting the expected weight from the weight-width chart upon the grid, indicating this with an arrow and a circle. In the sample shown, at "A" the child is slightly off the path from the disturbance of parental operation. At "B" the child suffered appendectomy nearly a year after growth slows. At "C" as growth increasingly lags the child is becoming disturbed.

of appendectomies according to their height and pelvic width.

It was found that 137 of the appendectomies were of average build: 58 were narrower for height. It was found that taller than average children exceeded by 15 cases shorter than average children. Wider than average children exceed slightly narrower than average. Thus if type of skeletal build is related to personality, and if personality determines in part the disease selected by the individual in his adaption to stress, apparently personality plays little part in the production of appendicitis *per se*. We regret that our cases were not typed according to Sheldon's method,[22] which, however, is too elaborate for routine school work.

In spite of this, one can often predict with considerable accuracy when using Wetzel grids that a child may become the victim of appendicitis. In the sample shown, the child has early disturbed rate of growth related to parental operation. It is an excellent wager in such a child that if in later life another chronic stress situation causes disturbance in speed of growth, when this disturbance is large enough, the child will itself suffer abdominal section when a still later acute stress occurs. Whatever it is that preselects the organ system attacked under stress, whether it be personality pattern, physiologic infantilism,[15] inherited psychological patterns, or organ inferiority, to mention a few of the theories, none seem to apply as much as a previous parental abdominal section causing developmental lag together with later stress sufficient to cause lag and an acute superimposed stress such as leaving home for the first time, etc.

We were surprised to find in both groups the paternal death rate so much greater than the maternal. In this regard it should be remembered that many widows of farmers choose to come into this university city, rather than go to a smaller non-educational centre.

Most striking was the fact that parental illness was five times greater among appendectomized children. Paternal illness seemed somewhat more common than maternal amongst the appendectomized, and maternal amongst the non-appendectomized. Enlistment of the father and more especially his return, seemed productive of appendectomy in the children, doubtless an indication of family adjustment stresses after years of separation. In all, potentially stressful events were twice as common amongst the appendectomized.

One cannot leave stress situations without at least a reference to attitudes. Known disturbed homes, with known immature attitudes, are often proved productive of appendectomy. In one disturbed home two laparotomies on the mother were followed in the following 18 months by 3 appendectomies on 3 of her 4 sons, only the eldest, who was away from home, escaping. Further, in the disturbed home a not unusual situation is to have the child give a history of tonsillectomy, at about 5 years, appendectomy at about 8 years, chorea or rheumatic fever at about 10 years, delinquency or serious educational difficulty at about 13 years.

Amongst these 263 appendectomies 40 individuals became educational or emotional problems. There were three cases of rheumatic heart disease, two suffered bed confinement for rheumatic heart disease, four had heart murmurs, four became enuretic, 14 complained of severe nightmares or night terrors, 15 became accident prone, two later had acute nephritis, 14 later were labelled neurotics and 4 developed serious speech difficulties.

It was felt that there was the probability that the appendectomized child might be operation prone. Upon study it was found that 1.5% of the controls suffered other operations besides tonsillectomy as against 2.8% in the cases of the appendectomized. However, 4 of the 7 operations amongst the appendectomized were herniotomies, and thus we felt the difference was without significance.

A typical Wetzel grid of an appendectomized girl is shown in Fig. 1. This child was the second of two in an upper socio-economic group. Her father had a gastric operation just prior to her first measuring at "A", and we attribute her developmental lead to this: 16 months later she is upon her expected auxodrome, where she remains for three and one-half years. Then, with no known stress except the gastric ulcer personality of the father and immunization for diphtheria, pertussis, and scarlet fever, she develops lag lasting 16 months. Appendectomy then eases her lag as her increased ACTH production is diverted from growth disturbance to the production of hypermineralocorticoidism and appendicitis. She is returning to her expected auxodrome when, 16 months later as her lag again increases

from as yet an unknown stress, she becomes a home behavioural problem at "C". We should emphasize that during her lag prior to "B" she enjoyed exceptionally good health, and at "B" she left home for the first time alone for a summer vacation.

We have modified our use of the Wetzel grid from that of Wetzel, as follows: we obtain from our weight-width chart the "expected" weight according to sex, age, height, and pelvic width. We plot this "expected", shown by a circle and an arrow, thus giving the channel the child should be following according to skeletal build. We use this plotting level as the level at which we begin the "expected" auxodrome. Many children will, for instance, follow channel A2 for some years, when clinical appearance and the weight-width plotting shows they should be in channel B1.

DISCUSSION

It would seem significant that 65.4% of the appendectomized had underlying stress situations, whereas only 21.1% of the controls had such conditions. One would expect that if Selye's general adaption syndrome has validity there could be seen in stressed children in our culture and civilization the following syndrome: stress —> tonsillectomy <=> appendectomy —> further trouble. That the appendectomized should so closely follow this syndrome is not remarkable when deviations from the expected upon the Wetzel grid are interpreted as due to stress, at the same time accepting that the origin of the stress is of little importance, and that stress inevitably, if present, will cause increased ACTH production. What occurs from then on apparently is determined by some such "preselection" mechanism as we have indicated, provided the stress is continued and enhanced sufficiently.

To further support Selye's general adaption syndrome, appendectomies should conform to the law of "limitation of energy", modified of course, by the "all or none response" of infancy.

What we mean is this: as is well known, the infant responds to external or internal stimuli in an "all or none" manner in which the adaption energy is transmitted through the cerebrospinal, autonomic, and endocrinal mechanisms. As the infant ages, control is acquired to some extent over all three mechanisms, only becoming lost when excessive stimuli exhaust it. At the same time, each stress situation constitutes a definite stimulus to the child, generating a definite amount of energy. As is known, with a stress situation, the child's reaction to previous stresses will determine which one of the three combinations of the three above mentioned mechanisms will be used for adaption. As a rule, all three of the above are used in part with one absorbing most of the adaption energy. Applying this limitation of the adaption energy concept to the condition of acute appendicitis what probably occurs is this: firstly, most of the energy is diverted to the endocrines. Growth is first of all affected, but a considerable part results in hypermineralocorticoidism and appendicitis and little is directed to the autonomic or cerebrospinal nervous systems. Therefore, the more acute the appendicitis the less would one expect to see behavioural troubles or symptoms of autonomic system imbalance at the time of appendectomy. In contrast, the subacute and chronic appendices should have part at least of their adaption energy, depending upon the strength of the stress situation, directed into the production of behavioural, education and other disturbances, a history of difficulty in management or of lessened school achievement being common.

In considering the probable mechanism whereby stress situations produce appendicitis, perhaps the findings of Michael[20] on the effect of brief stress are most significant. Michael found that brief stress caused a lymphocytosis; that this response was quickly exhausted, and that the lymphocytosis rapidly became a lymphopenia with a relative neutrophilic leucocytosis; and that the exhaustion lasted three or four days. He has suggested that the fraction, lymphocytes/neutrophils is an index of the relative hypermineralocorticoidism.

Selye previously had suggested that stress resulted in lymphopenia and increased production of immune globulin and of antibodies. It would seem unreasonable not to expect that the increased production of immune globulin and antibodies mentioned by Selye is not also finally exhausted by continuing stress. It would also seem unreasonable not to expect that the lymphoid changes seen in the blood stream do not exist also in the appendix. The appendix contains much lymphoid tissue.

Probably similar changes in the appendix occur, lowering the barrier to bacterial invasion, whilst at the same time the changes mentioned above assist. Beck *et al.*,[23] have recently reported upon the striking lack of any attempt to wall off infection in two cases of peritonitis induced by ACTH administration during the treatment of other conditions.

As the preselection phenomenon becomes more familiar through the use of Wetzel grids its importance increases. Apparently something occurs which causes subsequent hypermineralocorticoidism to be directed toward the specific organ system later affected. Consequently, a lesser degree of hypermineralocorticoidism is required to produce appendicitis than would otherwise be required.

The importance of the third stress is likewise apparently of importance, although its influence appears to be too brief to register upon the grids. With regard to the tonsil, probably much of what we have shown with the appendix applies.

In conclusion, may we quote Beck *et al.*

"In investigations of clinical and metabolic effects of adenocorticotrophic hormone (ACTH) and cortisone acetate, it is increasingly apparent that many of the common criteria employed in the diagnosis and evaluation of diseases are no longer valid." And Mote[23] "The comprehension of the rôle of the adrenal glands in health and disease in human beings has probably opened the largest single area of medicine that has occurred since the discovery of bacteria".

If one will accept the fact that stress may be other than bacterial in origin, and have equal force with bacterial stress in the causation of disease, and that when stresses are of differing natures, *i.e.*, emotional vs. bacterial, they have an augmentative effect much greater than when they are of the same nature, it seems possible to plow through the seas of promised uncertainties ahead with a confidence that otherwise will be lacking.

SUMMARY

1. 263 appendectomies were studied amongst 6,254 non-appendectomized school children.

2. The incidence of tonsillectomy was twice that of the controls, 34% suffering tonsillectomy prior to appendectomy and 27% of the remainder suffering tonsillectomy after appendectomy, with the probability that nearly 70% of the appendectomized children will suffer tonsillectomy before graduation in contrast to 25.3% tonsillectomized at present among non-appendectomized children.

3. Stressful events were twice as common amongst the appendectomized children.

4. It was found that other diseases of Selye's general adaption syndrome were more common amongst the appendectomized than amongst the controls.

5. Operation-proneness seemed higher amongst the appendectomized, but the cases of the latter were too few to be definitely significant.

6. The mechanism by which stress situations may end in appendicitis is briefly discussed.

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PNEUMOTHORAX AND INTERSTITIAL EMPHYSEMA IN ASTHMA*

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THE purpose of this presentation is to draw attention to the occurrence of pneumothorax, and interstitial emphysema, in asthma.

CASE 1

A male child, was admitted to the Children's Memorial Hospital, at the age of 3 years and 1 month, December 21, 1948 and died the following day. He had had several attacks of asthma during the course of the preceding 14 months. The attacks were always related to coincident respiratory tract infection. Scratch tests using common food and inhalant antigens were all negative. Prior to his last illness, there had been cough for two and a half days, with wheezing and laboured respiration for one day. The temperature was 101.4° F. on admission; it rose rapidly during the following 24 hours, reaching a peak of 107° F. rectally. An x-ray of the chest showed consolidation of the left upper and right middle lobes. The white blood cell count was 28,900. The administration of

* Read before Canadian Medical Association, Section of Allergy, June, 1950.

antibiotics, adrenalin, and oxygen, was followed by considerable temporary clinical improvement. About 24 hours following admission, early in the morning, the child had a mild generalized convulsion. He was cyanosed; and thereafter respiration continued to be more laboured and distress was severe. Subcutaneous emphysema of the chest wall was discovered, and an x-ray showed emphysema of the mediastinum. Aspiration of air from the mediastinum, administration of oxygen, adrenalin, bronchoscopic suction, and other supportive measures, failed to produce any material change in the general condition and death occurred about 8 hours after discovery of the emphysema. There was no pneumothorax.

Post-mortem examination showed massive collapse of the left lung; considerable emphysema of the major portion of the right lung, with some areas of atelectasis; interstitial emphysema of all areas of the mediastinum, and a mucous plug obstructing the left bronchus. The site of rupture causing the emphysema could not be demonstrated.

CASE 2

Mrs. S., a white female of Central European origin, aged 38 years, was free of asthma and vasomotor rhinitis until about the age of 36. At that time she developed severe bronchial asthma; there was no clinical evidence of sensitivity to any food or inhalant allergens; and intradermal skin tests were negative. Because of radiological, and some clinical, evidence of paranasal sinus disease, radical antrotomy was done, first on one side, which was followed by temporary disappearance of asthma, and later on the other side on recurrence of asthma, without benefit.

During the last year of her life she was in a considerable degree of respiratory distress most of the time and for the last few months, bedridden. On August 11, 1949, while dyspnœic, exhibiting the physical signs of chronic pulmonary emphysema, and widespread bronchial dry wheezing râles, she complained of pain localized in the left hemithorax. X-ray showed a partial left-sided pneumothorax. The pneumothorax disappeared, spontaneously, over a period of several days without further incident.

After a reasonably comfortable night, suddenly on November 12, about 8 a.m. she became extremely dyspnœic, and deeply cyanosed. Introduction of a needle into the left pleural cavity in the lower axilla resulted in escape of air under pressure greater than the pneumothorax apparatus would register. Some relief of dyspnœa and cyanosis followed, and an apparatus was attached to the thoracentesis needle, providing negative pressure. While air continued to escape through the needle, subcutaneous emphysema developed, in the chest wall about the thoracentesis, and also spreading up through the superior mediastinum over the face and neck. Death occurred in about five hours, with subcutaneous emphysema of face, neck, arms, and torso, as far as the inguinal ligaments.

At autopsy, the pathological diagnosis was as follows: (*a*) hyaline swelling of the bronchial mucosal basement membrane; (*b*) chronic exudative bronchitis, bronchiolitis, and peribronchial interstitial pneumonitis with eosinophil polymorphonuclear leucocytes present in the exudate; (*c*) bronchial mucous hypersecretion with massive mucous plugging of the bronchial tree, and mucus present in pulmonary alveoli in focal areas; (*d*) acute pulmonary emphysema with left (drained) pneumothorax, and interstitial emphysema of the lung, pleura, mediastinum, retroperitoneal tissues and the subcutaneous tissues from head to foot (Figs. 1 and 2).

CASE 3

D.A., a male, aged 29 years. This young man had asthma since the age of three years. He was admitted to the hospital April 10, 1948, because of pain in the right side of his chest. He had had mild asthmatic breathing for the preceding several days; and as he had had pneumothorax on at least two previous occasions, on the left side, he had become quite familiar with the symptoms of his condition. Clinical examination and x-ray showed the presence of air in the pleural cavity on the right side. On this admission the pneumothorax did not give rise to any inconvenience except a moderate amount of pain; there was no major displacement of the mediastinum, and no circulatory embarrassment or severe dyspnœa. With slight restriction of physical activity (he refused to be put to bed) expectorants, and bronchodilators, the pneumothorax disappeared in several days. Control in this case was unsatisfactory, and the patient declined any measures designed to obliterate the pleural cavity. X-rays suggested at one time during this episode, the presence of air in the mediastinum; but generalized subcutaneous interstitial emphysema did not develop.

While it is not now generally believed that tuberculosis is the primary underlying factor in all cases of spontaneous pneumothorax, the importance of asthma as a possible underlying factor is often overlooked. There is, in fact, evidence to suggest that some cases are clinically undiagnosed. In one instance[9] an asthmatic woman collapsed and died within 10 minutes of the onset of severe dyspnœa and cyanosis, the pneumothorax being discovered at post-mortem; in another[15] an asthmatic man died, with pneumothorax clinically unrecognized although x-ray showed pneumothorax present on admission to hospital over 24 hours prior to death. In our fatal adult case, x-ray several months antemortem showed a pneumothorax, which spontaneously disappeared, the film being taken because of sudden sharp pain localized to one side of the thorax.

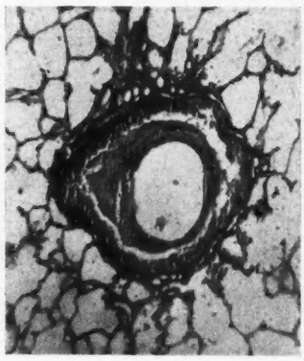

Fig. 1

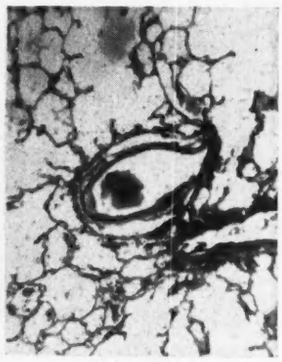

Fig. 2

Fig. 1.—Case 2.—A bronchiole is shown. The lumen is partly filled with mucus. In the upper part of the section, is shown an area containing eosinophilic exudate and small circular cavities. These represent air bubbles in the interstitial spaces, and under high power some appear to be in lymph vessels. **Fig. 2.**—Section of lung from Case 2.—In the centre of the field a vein is shown. Throughout most of its periphery, it is separated from lung tissue by a layer of air. The air is believed to spread along the vessels and bronchi to the hilum of the lung, and thence be widely distributed.

Myerson,[5] in 100 consecutive cases of pneumothorax found 3 asthmatic subjects. Hyde and Hyde[3] reported 63 cases of pneumothorax

5 of whom gave a history of asthma. Pneumothorax may occur in childhood; Rosenberg and Rosenberg, reviewing 18 cases of subcutaneous emphysema complicating asthma, found 7 in the first decade. In some cases, a clinical attack of asthma was in progress at the onset of the pneumothorax; in other asthmatic subjects asthma was not clinically present at the time of onset of pneumothorax.[3]

Many authors adopt a very sanguine attitude in offering a generally benign prognosis. Our own experience teaches us the folly of overlooking the seriousness of the condition; apart from the two here reported, four fatal cases have been recorded in the English and American literature in the last decade. We believe that the actual number, unrecognized, and unreported, is greater.

Pneumothorax, mediastinal emphysema, and subcutaneous emphysema, may co-exist, or, clinically, appear singly. It is likely that a combination of pneumothorax and mediastinal emphysema frequently exists, but the clinical and x-ray signs of one condition may render recognition of the other difficult. If the mechanism in humans is the same as Macklin showed in cats (where air introduced under pressure into the bronchial system, ultimately proceeds through a rupture within the parenchyma of the lung, along the vessels to the hilum and mediastinum, and thence rupturing the parietal mediastinal pleura, producing pneumothorax) then it is likely that both conditions frequently co-exist, one or other element predominating.

Occurrence of pneumothorax may be announced by sudden increase in dyspnœa, pain on one side of the thorax (recognized by the patient as different from the generalized soreness of the chest which accompanies an asthmatic attack) alteration in character of the cough, cyanosis, and collapse; mediastinal emphysema by subjective awareness of crunching or creaking in the chest, signs of circulatory embarrassment, and objectively by characteristic physical signs of the condition. Subcutaneous emphysema spreading through the superior mediastinal notch, should suggest the origin.

As Macklin points out, pneumothorax compresses the lung, assisting in control of the air-leak from ruptured alveoli into the interstitial pulmonary tissue. Development of pneumothorax may relieve pressure of interstitial air in the mediastinum and on the great vessels. Coronary circulation and heart action may be affected; and interstitial air in the lungs may seriously embarrass pulmonary circulation.

Prognosis.—Interstitial emphysema, mediastinal or subcutaneous and pneumothorax, are generally accorded a good prognosis. It would appear, however, that in asthma interstitial emphysema and pneumothorax present a less favourable prognosis because the asthmatic state tends to keep in effect the situation primarily responsible for the air leak.

Treatment.—Rest, and no mechanical interference with the pneumothorax are generally recommended; and in fact some cases recover rapidly under this regimen. In the face of increasingly deep cyanosis and collapse, the wisdom of attempting to provide some relief by partial reduction of pneumothorax tension, until co-existing broncheolar spasm and plugging is reduced, seems obvious. When pneumothorax is recurrent, obliteration of the pleural space by some of the available simpler techniques may be considered. Aspiration of air from the mediastinum may relieve mediastinal pressure. In view of the fact that both our fatal cases showed a high degree of bronchiolar plugging due to mucus, measures directed towards removing mucus are of the greatest importance. Hydration, iodides, relief of bronchiolar spasm, and, especially, prompt bronchoscopic aspiration, are probably of as great importance as control of pressure effects of interstitial emphysema or pneumothorax.

SUMMARY

Pneumothorax in asthmatics may be commoner than generally recognized; a sudden critical increase in dyspnœa, and cyanosis, or pain confined to one side of the chest should direct enquiry in this direction.

Pneumothorax and/or interstitial emphysema is a cause of death in asthmatics.

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MITRAL OCCLUSION DUE TO MASS THROMBUS OF THE LEFT AURICLE*

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EVANS and Benson (1948) have used the term *mass thrombus* to describe a clot that forms in the left auricle during life and by reason of its large size or its peculiar location impedes the flow of blood through the mitral orifice. This term includes *attached, pedunculated* and *ball* thrombi; avoids ambiguity in the definition of *ball thrombus*, and specifies obstruction of blood flow through the mitral valve as the important factor in its definition. Evans and Benson reviewed 46 cases of mass thrombus reported in the literature and added 6 of their own. Recently we have had the opportunity of studying clinically and at autopsy 3 cases of mass thrombus of the left auricle within a period of three months.

CASE 1

Male, aged 42. This patient had chorea at the age of 10 years. He remained well and worked at a vigorous occupation until 1943 when he was admitted to hospital dyspnœic and œdematous. A diagnosis of chronic rheumatic heart disease with mitral stenosis was made. He was given digitalis and changed his occupation to lighter work but continued to have ankle œdema, dyspnœa, and occasional bouts of hæmoptysis. In the period from 1943 to his final admission to hospital on December 19, 1949, he had frequent episodes of more severe congestive heart failure, often precipitated by upper respiratory infection. Auricular fibrillation was present from 1946. During an admission to hospital in 1947 he complained of aching pains and numbness in both shoulders, not related to exertion, not relieved by nitroglycerine. During a later admission he experienced numbness of the thumb and first two fingers of the right hand, and reported that he had noted this symptom often.

His final admission to hospital was for the treatment of herpes ophthalmicus. At that time he appeared to be in borderline cardiac compensation. There was moderate orthopnœa, the heart was clinically enlarged, the rhythm was irregular due to auricular fibrillation, there were systolic and mid-diastolic murmurs audible at the cardiac apex, the liver was not palpable, there was no ascites or peripheral œdema, the blood pressure was 110/80. An x-ray of the chest revealed a heart of mitral configuration.

The herpetic eruption slowly subsided and he presented no outstanding cardiac symptoms until 6 weeks after admission, when he developed dyspnœa and cyanosis despite the continuance of bed rest, digitalization, use of mercurial diuretics and a low salt diet. He complained of pain in the right chest anteriorly, and developed nausea, vomiting and hæmoptysis. The blood pressure fell to 90/50, the pulse increased to 110. It was not understood why he had lapsed rather suddenly into difficulty while still at bed rest. X-ray of the chest showed marked pulmonary congestion but no evidence of pneumonic consolidation or pulmonary infarction. Arterial and venous blood cultures were negative.

His condition deteriorated within the next few days. He became extremely orthopnœic and cyanotic, the hands and feet were cold and blue, the pulse was thready and the blood pressure unobtainable, the murmurs at the cardiac apex were inaudible and the sounds indistinct because of coarse moisture in all lung fields up to the level of the clavicles. The signs of right-sided heart failure were conspicuously absent. There was no distension of neck veins, no ascites, peripheral œdema or hepatomegaly. Therapeutic measures were of no avail and he died on February 8, 1950.

At autopsy the heart weighed 585 gm. There was dilatation and hypertrophy of the left auricle, right ventricle, and right auricle. The aortic valve was moderately stenosed, the valve leaflets were calcified and fused. The mitral valve was markedly stenotic, the valve cusps were firm, thickened and nodular, the edges of the cusps could not be approximated, the chordæ tendineæ were shortened and thickened. The left auricle contained a mass of antemortem thrombus material which was fixed to the wall and occupied most of the auricular cavity. It extended up the posterior wall and surrounded the orifices of the pulmonary veins. In its deeper portions near the auricular endocardium it was yellow in colour and appeared organized. Only narrow channels were present to allow blood flow from pulmonary veins to the mitral valve orifice. The coronary arteries were normal; there were infarcts in the right lung and left kidney.

CASE 2

Male, aged 46. This patient gave a history of chorea at the age of 5 years and was known to have been left with a damaged heart. At the age of 39 years he noted dyspnœa on exertion; physical examination at this time revealed mitral stenosis with auricular fibrillation. He continued with his occupation as a school teacher until the age of 42 years when he was forced to take a more sedentary position because of shortness of breath. Two years later he developed swelling of the ankles and following undue activity was hospitalized with massive peripheral œdema and ascites. In the year prior to his final admission to hospital on July 29, 1949, he had persistent ascites which required paracentesis every three weeks.

On examination the patient was orthopnœic, the neck veins were distended, the heart was enlarged, the rhythm was irregular due to auricular fibrillation, systolic and mid-diastolic murmurs were audible at the apex, the second sound in the pulmonary area was loud and followed by a short early blowing diastolic murmur considered to be the result of pulmonary valve insufficiency (Graham-Steel murmur). The blood pressure was 90/70, there were moist râles at the right lung base, the liver edge was palpable 3½ inches below the costal margin, there was massive ascites. X-ray of chest revealed cardiac enlargement, mainly involving left auricle and right ventricle, prominence of the pulmonary artery, calcification of the mitral valve, and a small aortic knuckle. Cardiac catheterization studies with fluoroscopy confirmed the presence of a widely dilated pulmonary artery and a high pulmonary artery pressure (Fig. 1). The clinical diagnosis at this time was rheumatic heart disease, mitral stenosis, with pulmonary insufficiency, and cardiac cirrhosis.

During his course in hospital he remained orthopnœic and required frequent paracenteses for recurrent ascites. He was given digitalis, mercurial diuretics and protein supplements to the diet. He continued to receive alpha tocopherol 375 mgm. daily, which he had been taking

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prior to admission to hospital. On the morning of the 204th hospital day he complained that his legs felt paralyzed, they appeared cold, blue, and lifeless. Blankets failed to warm him. On examination later that day there was marked orthopnœa and extreme cyanosis of the face and extremities. He was unable to move his limbs, radial and tibial pulses were not palpable, blood pressure was unobtainable. He was mentally alert and had no pain. The first heart sound could not be heard, the second sound was loud, there was no evidence of pulmonary œdema. The impression was gained that he died from the periphery by a slow process of vascular shut down. Because of the slowly developing, severe, symmetrical cyanosis of face and extremities, the clinical diagnosis of mass thrombus of the left auricle was made.

At autopsy the heart weighed 538 gm. There was dilatation and hypertrophy of the left auricle, right ventricle, and right auricle. The aortic valve was normal. The pulmonary artery was dilated and the pulmonary valve ring wider than normal. The mitral valve was

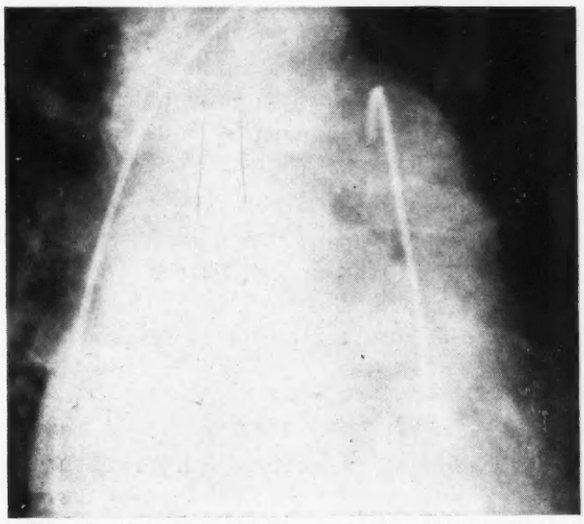

Fig. 1. (Case 2).—Male, aged 46. Mitral stenosis. Cardiac catheter in dilated pulmonary artery. Auscultation revealed early diastolic murmur. Aortic valve normal at post mortem.

severely stenosed, the valve leaflets were fused, nodular, and calcified, the valve orifice measured only 1.0 x 0.5 cm. The most outstanding feature was the presence of a mass of thrombus material almost completely filling the left auricular cavity measuring 8 x 6 x 3 cm. It was adherent to the auricular endocardium, and partially occluded the orifices of the pulmonary veins and the mitral valve. That portion of the thrombus attached to the posterior wall of the auricle appeared to be older and partially organized; the central portion hanging down toward the mitral orifice was relatively fresh. The coronary arteries were normal.

The lungs showed chronic passive congestion but no pulmonary œdema. The branches of the pulmonary artery were dilated and contained atheromatous plaques. There were bilateral healed infarcts of the kidneys. The liver was small, hard and granular in appearance.

CASE 3

Female, aged 48. This patient had rheumatic fever as a child, requiring a long period of bed rest. She had no symptoms referable to the cardio-vascular system until one month prior to admission to hospital, when she developed dyspnœa, anorexia, loss of strength, chills and fever. When examined by a physician two weeks before admission she was orthopnœic, the heart was enlarged, the pulse was irregular, the temperature was 103° F. On the day of admission she complained that her legs felt paralyzed and painful. She was extremely dyspnœic and cyanotic, the temperature was subnormal, the heart was clinically enlarged, the pulse 128 and the rhythm irregular. There was a systolic murmur in the aortic area transmitted to the neck vessels and there were systolic and mid-diastolic murmurs in the mitral area; the blood pressure was 92/60, the liver was enlarged, there was pitting œdema of the legs. Both upper and lower extremities were cold and cyanotic, radial and tibial pulses were barely palpable. An electrocardiogram revealed the heart rhythm to be sinus tachycardia with nodal extra-systoles.

Her condition deteriorated rapidly, the temperature remained subnormal, the arms and legs became more cyanotic and the pulses no longer palpable, the tip of the nose and cheeks were cold and blue, the blood pressure was unobtainable; only a systolic murmur could be recognized at the cardiac apex. She died 32 hours after admission to hospital. The clinical diagnosis was rheumatic heart disease with aortic stenosis, mitral stenosis, sub-acute bacterial endocarditis and mass thrombus of the left auricle.

At autopsy the heart weighed 425 gm. The aortic valve was stenotic, the valve cups were thickened and calcified. On the upper border and inferior surface of the valve cusps there were friable grey vegetatians which contained masses of bacteria on microscopic examination. The mitral valve was stenotic, the valve leaflets were thickened and fused, the chordæ tendineæ were shortened. There were grey vegetations on the posterior cusp of the valve and a superimposed mass of fresh ante-mortem thrombus material which extended up along the posterior wall of the left auricle and was continuous with similar thrombus material in the left auricular appendage. With the left auricle unopened, the mass of thrombus material was seen to fill almost completely the mitral orifice. Culture of the vegetations on the heart valves grew *Strep. viridans.*

The lungs showed chronic passive congestion and moderate pulmonary œdema. There were two small recent infarcts in the left kidney. Microscopic examination of the kidneys showed several areas of focal embolic glomerulonephritis.

DISCUSSION

In these three cases of mass thrombus of the left auricle, mitral stenosis was present in each.

In two of the cases auricular fibrillation was known to have been present for several years before death. It is believed that slower movement of blood because of the absence of auricular systole in fibrillation contributes to the formation of thrombus in the left auricle. This is supported by the data of Evans and Benson; auricular fibrillation was present in 43 of the 52 reported cases. In our 3rd case with sinus rhythm, the vegetations of subacute bacterial endocarditis appeared to provide a base for the deposition of the thrombus material.

The clinical diagnosis of mass thrombus of the left auricle was made in two of these three cases a few hours before death. It was suspected because of the appearance of severe symmetrical peripheral ischæmia and cyanosis in patients with known mitral stenosis (Fishberg 1940). There appeared to be no other specific clinical symptoms or signs which could not have been attributed to the valve lesion or the presence of congestive heart failure. It is interesting that two of the patients complained that their legs felt paralyzed, and indeed, their extremities did look cadaveric. In neither of these cases was there post-mortem evidence of peripheral arterial embolism.

In two of our cases the disappearance of heart sounds and murmurs was noted, (Schwartz and Biloon 1931, Schiller 1935), coincident with the development of symmetrical cyanosis and peripheral vascular failure. In the 3rd case coarse moisture in the lungs prevented an accurate assessment of changing murmurs. In these cases the diagnosis was not made until shortly before death, and in all three recent thrombus formation was observed at post-mortem. The clinical picture observed in these cases according to Fishberg (1940) may be caused by a very tight mitral stenosis, in the absence of mass thrombus, in any event it is due to mitral occlusion, the severity of the signs depending on the degree of occlusion. Intermittent occlusion due to a ball valve action has been reported.[1] The mechanism is considered to be severe peripheral vaso-constriction following the serious fall in cardiac output and would account for the typical sequence of events noted in these cases including the disappearance of sounds and murmurs, fall in blood pressure and cardiac pain emphasized by Evans and Benson as of importance in the diagnosis. In our cases cardiac pain was not a feature and in the 2nd and 3rd cases this was particularly sought once the diagnosis had been made clinically. In the 1st case, chest and arm pain had been present but this was not of a cardiac nature.

In a study of 186 cases of mitral stenosis Hay and Levine (1942) have shown that thrombi occur in the left auricle in 49% of cases with auricular fibrillation and in 14% of cases with regular rhythm, exclusive of bacterial endocarditis. In view of these observations and since death often occurs in cases of mitral stenosis in a sudden and unexpected or unexplained manner, but with the picture of peripheral collapse, it is remarkable that mitral occlusion is rarely considered to be the cause of death. It is therefore possible that many cases of mitral stenosis terminate as mitral occlusion due to plugging of the narrowed mitral valve by thrombus which may not be found *in situ,* due to post-mortem changes, manipulation, etc., at autopsy.

It is interesting to note that in Case 2, the patient, who died of the same cause within the same week, and who showed remarkably similar findings at post-mortem to Case 1, had received alpha tocopherol for a period of 18 months, up to the day of death.

SUMMARY

1. Three cases of fatal mitral occlusion due to mass thrombus in the left auricle, two of which presented a typical clinical picture diagnosed as mitral occlusion prior to death are described.

2. In these cases cardiac pain was not a feature.

3. Alpha tocopherol was ineffective in preventing the development of mass thrombus. Two cases with a long standing history of mitral stenosis ran parallel courses to a fatal termination due to mass thrombus of the left auricle, one of which received alpha tocopherol.

4. The probability of mitral occlusion occurring as the terminal event in mitral stenosis being more frequent than commonly regarded, is discussed.

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PEPTIDASES IN THE CEREBROSPINAL FLUID*

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THE first studies on proteolytic enzymes in cerebrospinal fluid were done in 1909 by Dochez.[1] Using denatured beef serum as substrate this author found no proteolytic activity in fluids from cases of tuberculous meningitis, although considerable activity was observed in cases of infection of the meninges with *Diplococcus lanceolatus* and with *Strep. mucosus*. Kaplan and co-workers[2] demonstrated the absence of trypsin and esterases in fluids in which the cellular and chemical findings were normal, but found considerable tryptic activity in fluids from cases of tuberculous meningitis and purulent meningitis.

With the development of synthetic peptides for use as substrates it has been possible to obtain quantitative clinical data on the activity of peptidases. Using the micro-titration technique of Grassmann and Heyde[3] the present authors[4, 5] showed that there exists in human serum a cobalt activatible peptidase which hydrolyses leucylglycylglycine at a rate which is uniform in health, but considerably increased in pathological conditions involving infection and tissue damage. It seemed interesting to investigate whether peptidases occur in cerebrospinal fluid, and whether their activity increases in disease.

MATERIAL AND METHOD

Cerebrospinal fluid was obtained from 21 patients suffering from a variety of conditions. In most cases the fluid was obtained during pneumoencephalography. The technique of Grassmann and Heyde[3] was used for measurement of the hydrolysis of the tri-peptides 1-leucylglycylglycine (LGG) and glycylglycylglycine (GGG). The experimental procedure was the same as that used to determine serum peptidase activity, which has been described in previous reports.[4, 5] The concentration of spinal fluid was 0.2 ml. per ml. of reaction mixture. The hydrolysis of LGG was carried out at a pH near pH 7.8, and that of GGG near pH 7.0. In all cases 0.001 M cobalt sulphate was used as activator.

RESULTS

In the majority of cases it may be seen that spinal fluid is considerably less active than serum in splitting LGG[4, 5] and GGG.* Only 7 of the 21 fluids studied had an activity greater than 1% per hour (see Table I). In the two cases in which there was considerable peptidase activity (one case of tuberculous meningitis and one case of acute purulent meningitis) the rate of hydrolysis was comparable to rates previously found in normal and pathological human serum.[4, 5] Fig. 1 shows the manner of compiling the data.

DISCUSSION

In reviewing the present findings and the observations in the literature on proteolytic enzymes in general it is impossible to conceive of a consistent theory to explain the presence or absence of peptidases in the cerebrospinal fluid. Nevertheless, Fruton and his co-workers have accumulated much circumstantial evidence that lymphocytes, and cellular elements related to lymphocytes, are the probable origin of peptidases.[6, 7] In the present study it has been shown that those spinal fluids which showed a high peptidase activity were fluids which contained a considerable number of white cells.

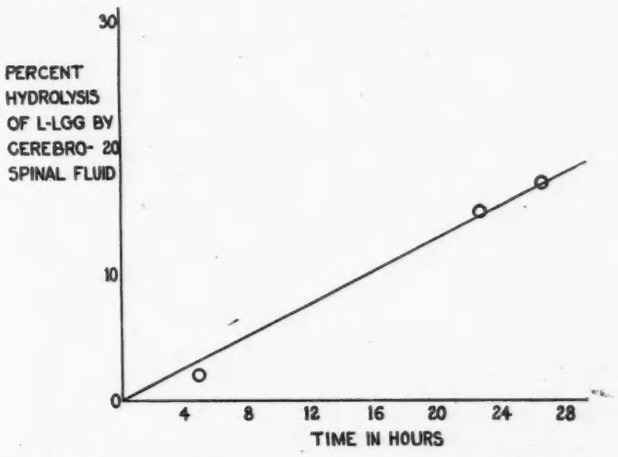

Fig. 1.—Hydrolysis of GGG by cerebrospinal fluid from a patient (L.A.) who had suffered a left occipital linear skull fracture.

SUMMARY

A study has been made of the capacity of cerebrospinal fluid to hydrolyse 1-leucylglycylglycine and glycylglycylglycine. The fluids were obtained from 21 patients, most of them undergoing pneumoencephalography. The micro-titration method of Grassmann and Heyde was used to determine enzymatic activity. In 7 of

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* Rate of hydrolysis of GGG by normal human serum is comparable with that of LGG (Unpublished data).

TABLE I.

HYDROLYSIS OF LGG AND GGG BY CEREBROSPINAL FLUID

Name	Age	Diagnosis	Cellular elements				Biochemistry			Hydrol of LGG %/hr.*	Hydrol of GGG %/hr.*	Remarks
			W.B.C./ c.mm.	% Poly.	% Lymph.	R.B.C./ c.mm.	Proteins mgm. %	Sugar mgm. %	Chlorides mgm. %			
B.A.	23	Idiopathic epilepsy					29.0			0.9		
B.A.K.	21	Anxiety neurosis					25.0				0	
B.R.	4½	Tuberculous meningitis	305 203	21 11	79 89	0 0	287.0 284.0	34.0 51.4	382 369	 1.8	3.0	Specimens taken 1 week apart.
C.L.	11	Focal cerebral seizures					24.0			0		
C.A.R.	17	Cerebral concussion contusion left temporal	3			56				1.6		
C.O.	42	Presenile dementia, diabetes mellitus	0			0	38.0			0		
M.O.	54	Acute purulent mastoiditis and meningitis	1140				136.3	46.0		15.5	17.0	Hydrolysis of LGG and GGG by serum: Normal (3 days later)
C.R.	10	Tuberculous meningitis	93		Nearly 100		316.0	30.8	390	3.9	5.5	Sept. 8/48 } Acid-fast bacilli
			90		Nearly 100		203.0	37.5	394	6.8		Sept. 14/48 } observed in smears.
			100	17	83		214.0	34.0	415	5.5		Sept. 21/48 }
										6.0		Sept. 29/48 No acid-fast bacilli
D.A.	31	Chronic encephalopathy								0.3		
E.D.	7	Mental deficiency				1	14.0			0.7		
K.Y.	14	Undiagnosed disease of central nervous system with periodic unconsciousness					27.0			0.5		
L.A.	30	Linear skull fracture, left occipital					64.0			0.6		
L.E.	—	Meningococcal meningitis								0.5		
L.E.R.	49	Idiopathic epilepsy					47.0			0		
L.L.	3½	Tuberculous meningitis	135	72	28	91	174.0	46.0	394	1.1	1.2	Acid-fast bacilli observed in smear.
McC.	2½	Hydrocephalus					47.0			1.3		
R.O.	18	Linear skull fracture, cerebral concussion and contusion	1–3				76.0			1.0		
S.N.	42	Menière's syndrome								0		
H.A.	51	Epileptic focal seizures (cause unknown)									1.2	
D.A.Y.	39	Depressed fracture, left temporo-frontal region					24.0				0	
Y.O.	17	Slight head injury followed by a single petit mal seizure									0	

*% per hour of the hydrolysis expected on the complete splitting of one peptide linkage.

the 21 fluids studied, the rate of hydrolysis of the tri-peptides exceeded 1% per hour. In one case of tuberculous meningitis it exceeded that of normal serum. These findings may be tentatively explained on the basis of Fruton's theory that peptidases derive from cellular elements, particularly white blood cells.

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SARCOID-LIKE ERUPTION FOLLOWING VITAMIN D THERAPY FOR ARTHRITIS*

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BOECK'S sarcoid and systemic sarcoidosis have been extensively studied. Besnier,[1] Boeck,[2] Schauman,[3] Pautrier,[4] Michelson,[5] Longcope,[6] and Thomas,[7] are among the numerous authors who have contributed to its better understanding. Various hypotheses have been suggested regarding the possible etiology of sarcoid and sarcoidosis. Relationship between sarcoidosis and tuberculosis is still debated. The favourable response,[8, 9, 10] of the sarcoid group to vitamin D_2 seems to be in favour of a tuberculous relation.

The following two cases have clinical and histo-pathological features of sarcoid, but appeared after the use of vitamin D for arthritis.

CASE 1

C.L., a 50-year old woman presented herself, January 5, 1948, on account of an eruption, located on the face, the shoulders and the upper extremities. The lesions, which had appeared two months previously consisted of numerous pea-sized nodules (Fig. 1). Their consistency was firm and their colour pink-brownish. No subjective symptom was present.

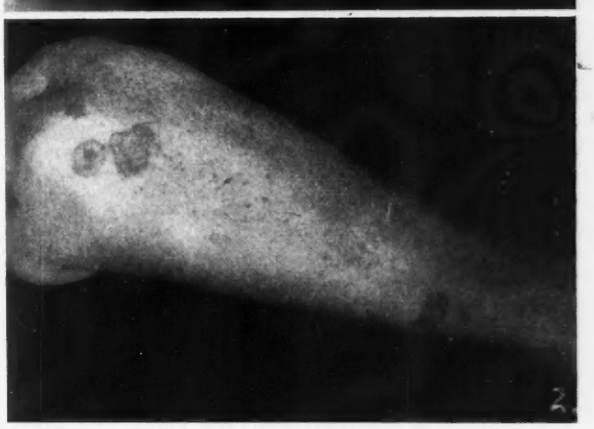
Upon questioning the patient, she mentioned that in the last few months she went to see her family doctor for arthritic pain located mostly in the large joints. She was then recommended to take 9 pills a day of radiostol (vitamin D). Ten days later she stopped taking this medication on account of the appearance of the eruption.

Physical examination revealed no other abnormality than the skin manifestations. There was no personal or family history of tuberculosis. The tentative clinical diagnosis being very doubtful, even if the nodular eruption looked like sarcoid, a biopsy of one lesion was proposed and accepted by the patient.

Biopsy report.—The skin examined shows a slightly atrophic epidermis and in the corium a small focus of epithelioid cells arranged in anastomosing strands separated by collagen. Here and there these epithelioid cells show a vague follicular structure. Some are in mitosis and a few are multinucleated, forming small giant cells Figs. 3 and 4. The general aspect is that of an intradermal epithelioid reticulosis, akin to Boeck's sarcoid. The same specimen was examined by Dr. Wilbert Sacks from New York, who believed that it is Boeck's sarcoid.

Chest x-ray was normal, except for exaggerated visibility of right lower bronchi.

White blood count, 9,000; P.N., 65%; P.E., 2%; lymphocytes, 26%; monocytes, 7%; Arneth formula: 19-34-39-7-1.



Tuberculin patch test, light and delayed positive (xx) reaction after 72 hours. The clinical aspect of the lesions and the biopsy reports were in favour of a diagnosis of a sarcoid-like eruption. The patient was then advised only to reduce her activities.

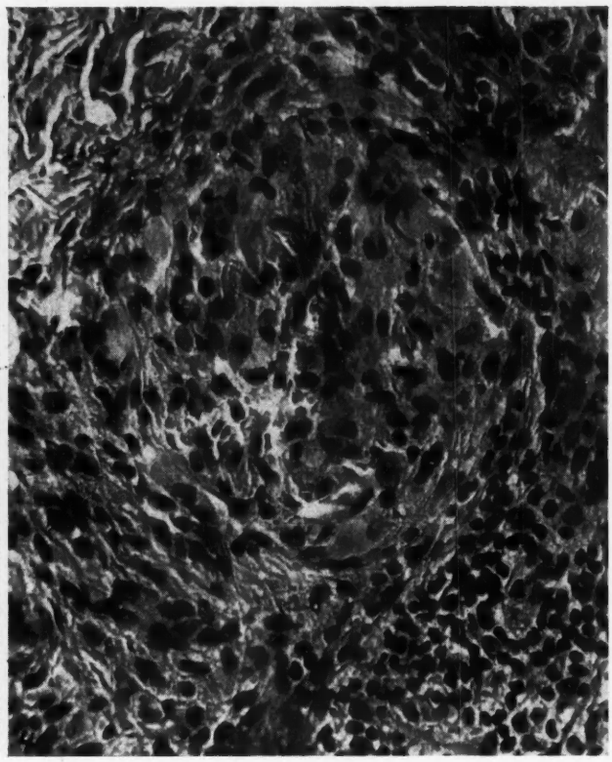
Course.—The patient was seen every three weeks for two and a half months, and there was a slow improvement of the skin lesions. Two other chest x-rays showed no lung involvement. Six months after the first consultation, the lesions were hardly seen. They left no scars.

The patient, as recommended, came back six months later and her skin was normal. There was no trace of the previous skin eruptions. Another chest plate was negative. Since then, regular reports from the patient regarding her skin and general health conditions are very satisfactory.

CASE 2

A.B., a woman aged 56, was first seen on November 3, 1947, for nodular lesions on both forearms and hands. These lesions had appeared fifteen days previously. They

* Presented at the Third Annual Meeting of the Canadian Dermatological Association held in Quebec, June 9 and 10, 1950.



were red, flat-topped nodules, round, oval and even linear in shape (Fig. 2). Their consistency was firm and they were slightly painful at pressure.

The patient stated that she had been taking vitamin D (osto-forte) for a month and a half on account of arthritis of the left knee. Since 1949, she has been hospitalized three times with the following diagnosis: obesity, cardio-renal insufficiency, chronic myocarditis, arthritis of the knees, chronic rheumatism and scabies. During hospitalizations, blood counts, blood urea tests, urine examinations and blood serology were normal. There was a family personal history of rheumatism, but none of tuberculosis.

On November 26, 1947, a biopsy of a nodule on the left forearm was taken. The report was as follows: The lesions are purely intradermal and consist of small nodular formations made up of short strands of epithelioid cells. In spots these cells show a vague follicular arrangement. A few are in mitosis and some contain two or three nuclei, giving the aspect of small giant cells. Furthermore, around a few capillaries, there is loose lympho-reticular cell infiltrate (Figs. 5 and 6).

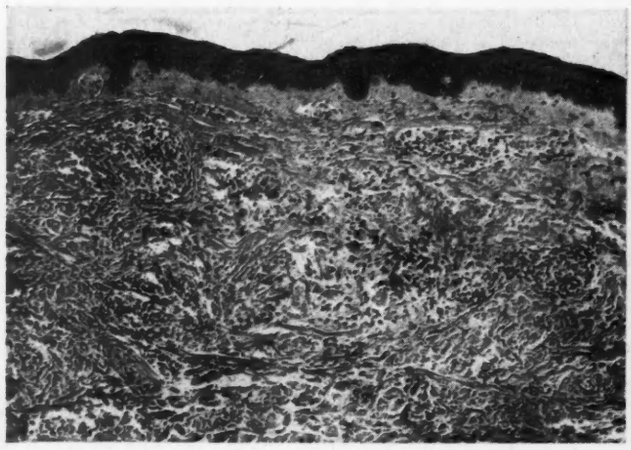
Diagnosis.—Epithelioid reticulosis of the derma somewhat akin Boeck's sarcoid, and perhaps the early form of this disease.

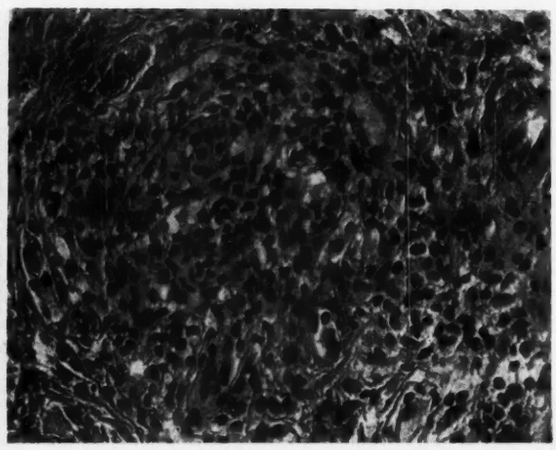
An x-ray of the chest was negative except for the possibility of an enlarged gland near the trachea.

Course.—The nodular lesions increased in size and in number during the following five months. Their total number was 33 in March, 1948. During that period, the patient was taking vitamin D in the form of ertron. In September, 1948, ten months after the first consultation, there was no improvement in the eruption. Some of the nodular lesions became confluent, taking on a vague aspect of granuloma annulare by their annular configuration. At that time, ertron was discontinued, and the patient was recommended to take vitamin D_2 in alcoholic solution following Charpy's method. Three weeks later, new lesions appeared, and some of the old lesions seemed to be more active. In December, 1948, all medication was stopped. In March, 1949, the lesions were still present, but no new lesions had appeared. In August, 1949, eight months after vitamin D was discontinued, the eruption had completely disappeared.

COMMENTS

These two cases of sarcoid-like eruption seem to have been caused by vitamin D. In the first





case, the lesions disappeared spontaneously and slowly after the cessation of vitamin D. In the second case, the lesions increased as long as the patient was taking vitamin D but disappeared also spontaneously a few months after it was stopped.

These two patients presented only skin lesions, and the clinical as well as the pathological features of the eruptions were somewhat like early lesions of Boeck's sarcoid. As long as we know so little about the etiology of the sarcoid group, we may assume that lesions very much related to that group may appear after the use of vitamin D. It would seem also that such an eruption would be seen only in patients with special backgrounds. Both cases presented here had a personal and family history of arthritis and rheumatism.

The mechanism of action of vitamin D in giving rise to this eruption is hardly understood. Medical literature, as far as we know, does not mention any similar eruption due to vitamin D. Otherwise, a few authors have reported the beneficial effect of vitamin D in Boeck's sarcoid and sarcoidosis.

CONCLUSIONS

Two cases of sarcoid-like eruption are presented.

In both patients, the clinical and pathological aspects of the eruption were closely related to the sarcoid group.

The eruptions appeared after the intake of vitamin D.

The spontaneous disappearance of the lesions followed the discontinuance of vitamin D.

We are indebted to Dr. Carlton Auger, professor of Pathology, Laval University, for his help regarding the pathological interpretation of the skin specimens.

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LUPUS ERYTHEMATOSUS
The Effect of Cortisone on the "L.E." Phenomenon in Lupus Erythematosus

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PATIENTS suffering from acute disseminated lupus erythematosus have been reported to show abnormal elements in their heparinized bone marrow by Hargraves[1] of the Mayo Clinic in 1948. Other investigators have confirmed this observation. Berman *et al.*[2] have reviewed the subject and outlined a procedure similar to the one we are using here.

The so-called "L.E. cells" are found in stained smears of fresh normal guinea pig bone marrow which has been mixed with plasma (or serum) of a patient suffering from an exacerbation of acute lupus erythematosus. The typical L.E. cell is a young neutrophil containing an amorphous, spherical polychromatic mass within its cytoplasm (Figs. 1, 2, 3, 4b). There are other manifestations of the phenomenon which are apparently related to the severity of the disease. The commonest of these are rosettes of granulocytes about single spherical masses (Fig. 4a) or about unorganized dark masses (Figs. 5, 6).

The formation of the L.E. cell, to the best of our knowledge, is not understood clearly. However, Haserick[3] has indicated by electrophoretic studies of plasma that the inciting factor is probably present in the gamma globulin fraction of the plasma protein. No attempt will be made in this report to discuss the mechanism or the specificity of the phenomenon because further investigations here are not ready for publication.

The case which came to our attention on June 24, 1950, was a 28-year old, white male electrician, employed by a paper mill. He was admitted to Sunnybrook Hospital complaining of shortness of breath, painful joints, loss of weight, and a rash on the face. He had apparently enjoyed good health prior to January, 1950, except for a specific urethritis in 1938, a severe post inoculation reaction characterized by severe arthralgia in July, 1942, and bronchopneumonia in November of the same year. In the early part of 1950, he consulted his physician on several occasions regarding joint pains but no significant physical findings were elicited. Finally, in May, he became quite ill with fever, arthralgia, loss of weight and a leukopenia (4,700). After a transient improvement, he suffered an acute exacerbation of all symptoms early in June. He had chills, conjunctivitis, photophobia, gingival hæmorrhages, a diffuse erythema-

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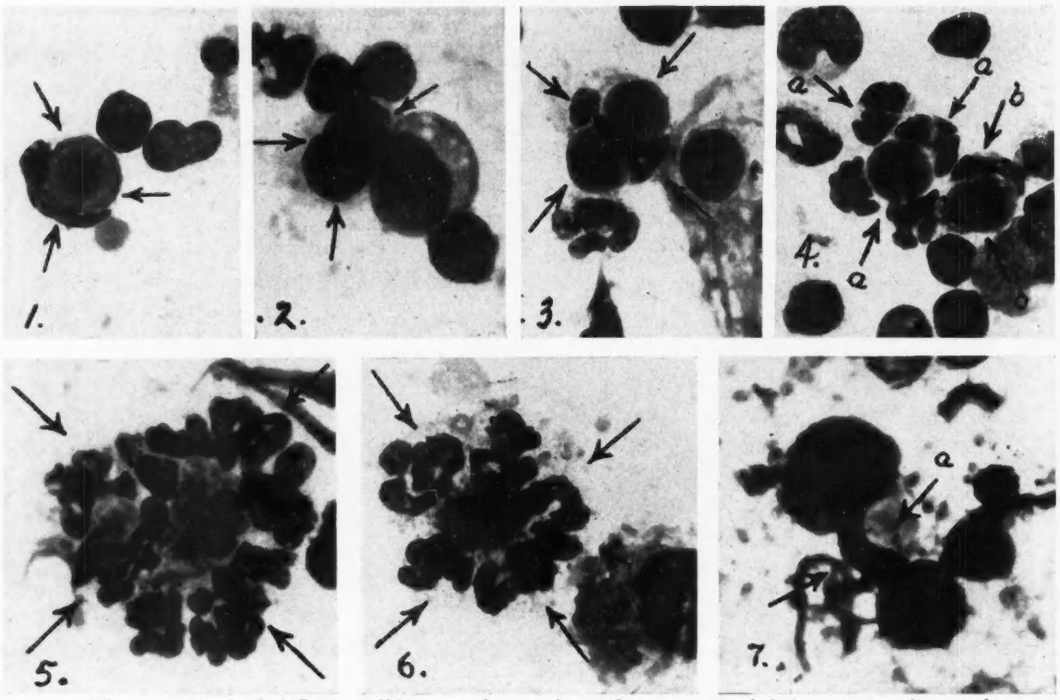

Fig. 1.—Typical "L.E. cell", a polymorphonuclear neutrophil in which the nucleus appears to be embracing a spherical smoky intracellular mass. **Fig. 2.**—Typical "L.E. cell" having a more basophilic inclusion. **Fig. 3.**—An "L.E. cell" with "twin" amorphous masses. **Fig. 4.**—A rosette of four neutrophils (a) about an amorphous mass. Note the typical "L.E. cell" (b) and free masses in the same field. **Fig. 5.**—A large rosette of neutrophils around what appears to be cellular debris. **Fig. 6.**—A rosette of neutrophils around basophilic filamentous material. **Fig. 7.**—The only "L.E. cell" found after cortisone therapy. Note the markedly autolyzed intracellular mass (a).

tous rash on the face and neck, and is reported to have raised blood streaked grey sputum.

The physical examination revealed a critically ill, dyspnœic, emaciated male with the blotchy red rash above the collar line, ill-defined lesions of the soft palate, and tachycardia. There were coarse tremors of the hands associated with the wasted tender muscles.

The laboratory investigation disclosed a trace of albumin and a few pus cells in the urine. Examination of the blood showed the hæmoglobin to be 11.7 gm. %, the erythrocyte count 3.7 million, the leucocyte count 4,000 with a differential count of 83% neutrophils, 16% lymphocytes, and 1% monocytes. The erythrocyte sedimentation rate was 105 mm. in one hour (Westergren). The standard Kahn and Wassermann, and the serum agglutination reactions were negative. The total serum protein was 6.35 gm. %, composed of the following fractions: albumin 4.55; globulin 1.80; euglobulin 0.62; pseudoglobulin 1.18; 13.5% globulin 0.15; fibrinogen 0.73 and fibrin 0.69 gm. %.

On clinical grounds alone, it was difficult to differentiate between acute disseminated lupus erythematosus and dermatomyositis. As a diagnostic aid, the procedure for demonstrating the L.E. phenomenon was carried out on June 27 and again on July 4. Examination of the stained smears on these dates disclosed 38 and 64 typical L.E. cells (Figs. 1, 2, 3, 4b) per 500 polymorphonuclear leucocytes. Rosettes about many otherwise free amorphous masses (Fig. 4a) were also present. A biopsy of the skin of the neck revealed histological features compatible with acute disseminated lupus erythematosus (Fig. 8).

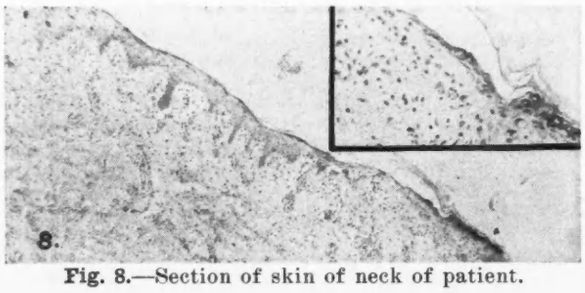

Fig. 8.—Section of skin of neck of patient.

On July 5, 1950, intramuscular cortisone treatment was started. Five days later, after he had received a total of 1,500 mgm., the clinical improvement was remarkable. The L.E. phenomenon was sought again and on July 10 only one partially autolyzed L.E. cell (Fig. 7) per 500 granulocytes and some free amorphous masses were found. Further search was made on July 11 when no L.E. cells were seen but the amorphous masses were still present. This, we believe, is due to an alteration in the L.E. cell producing factor and is associated with a remission of the disease.

SUMMARY

A case of acute disseminated lupus erythematosus is recorded wherein the demonstration of the "L.E." phenomenon was an aid in diagnosis. Associated with clinical improvement following cortisone therapy there was a marked decrease in the number of "L.E. cells" and an alteration in the quality of the abnormal amorphous intracellular masses.

The photomicrographs were produced by the Medical Art Department, Sunnybrook Hospital, Toronto.

We wish to express our thanks to Dr. D. C. Graham for the clinical history of the case.

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LEPTOSPIROSIS ICTEROHÆMORRHAGICA OR WEIL'S DISEASE*

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THE first successfully treated case of *Leptospirosis icterohæmorrhagica*, or Weil's disease, to be recorded in Canada occurred in a sewer worker admitted to the Montreal General Hospital during the month of November, 1949. The only instances of this disease heretofore reported in Canada, two in number, were recognized in Toronto in the years 1926[1] and 1940.[2] Both of these patients died. Over 300 cases have been reported in the literature of the United States up to March, 1950.

Since it is apparent that rats in Canada's two largest cities are infected with this disease which carries a high mortality for man, and which can be transmitted readily to him by mere contact with their excreta, it seems desirable to draw attention to the possibility of additional cases and to outline briefly the treatment and the laboratory methods by which the diagnosis is established.

Weil,[3] in 1886, described a type of infectious jaundice which he presented as a new entity. The etiological agent was not known. In 1915 Inada and Ido[4] in Japan and simultaneously Uhlenhuth and Fromme[5] in France identified a spirochæte as the cause of Weil's disease, which Noguchi[6] later named *Leptospira icterohæmorrhagiæ*. It was proved that rats were the carriers and were usually the source of human infection. Other species of leptospira have since been identified, one of which, *L. canicola*, is carried by dogs[7] and produces a human disease very similar to Weil's disease. Only these two species of Leptospira have been isolated in North America.

CASE HISTORY

A white male of 26 years was admitted to the wards of the Montreal General Hospital on November 7, 1949. He complained of the sudden onset of fever and chills, malaise and weakness, three days previously. The day before admission he developed a cough, muscle pains, most marked in the abdomen and legs, and an intense headache. His eyes had become very red and sore, and blisters had developed on his lips. The only helpful clue in his past history was the fact that for the previous eight months he had been working in the sewers of the City of Montreal. He wore no gloves and admitted that he usually had some abrasions on his hands. There were many rats in these sewers and he had on more than one occasion killed them.

On examination the patient was a well developed male, looking his stated age. He appeared very ill. His temperature was 105° F. The sclera were markedly injected and there were large subconjunctival hæmorrhages, but no exudate. In artificial light, icterus was not evident. Extensive herpes labialis was present. The mouth was filled with sordes but one characteristic petechia and several doubtful ones were seen on the soft palate. The lungs were clear. The heart was not enlarged, but there was a grade 2 systolic murmur best heard in the pulmonic area: pulse 120; blood pressure 118/70. The muscles of the abdominal wall and the legs were intensely tender. The abdomen was otherwise unremarkable, the liver showing no tenderness or enlargement. Deep reflexes were equal and active and there was no neck stiffness or Kernig. There was a slight generalized lymphadenopathy. Red cell count was 3,700,000 with 14,000 white cells and a differential count of 91% polymorphonuclear leucocytes and 9% lymphocytes. There was a trace of albumen in the urine.

Course.—Cultures were taken from the eyes, blood and sputum. As the prostration was so great, intramuscular procaine penicillin 400,000 units was administered immediately and repeated each day. By noon of the second day in hospital, the fifth day of disease, the fever had fallen to 100.4° F. Jaundice had not been evident on admission, but had developed the following day. Râles had developed at the left lung base. Blood was collected for culture and other investigations. The patient started to cough up bright red blood in a sputum that contained no pus cells. X-ray examination of the chest revealed a dense confluent infiltration from the second to the fifth rib anteriorly, obscuring the cardiac shadow on the left, with a patchy infiltration of the right. Because of the possibility of a Friedländer's pneumonia, 4 grams of streptomycin per day were added to the penicillin. The stool was negative for bile. On the sixth day of the disease the patient felt well. All signs of toxicity had disappeared but jaundice progressed, the serum bilirubin rising to 2.6 mgm. %. The herpes became hæmorrhagic. Hæmoptysis continued. The blood urea nitrogen was 34 mgm. % and the urine showed some albumen with a few red and white cells. The following day the cellular elements had risen to 10 of each. The jaundice increased but the patient continued to improve symptomatically. He was afebrile from the seventh day of the disease. On November 12, another x-ray film of the chest revealed that the infiltration described five days before had disappeared. On November 14, the serum bilirubin had risen to 7.2 mgm. %; the cephalin flocculation was 4 plus, the alkaline phosphatase was 6 King Armstrong units, the prothrombin time 24 seconds and the Takata-Ara negative. From this time the course was one of uninterrupted recovery. By November 18 the bilirubin had fallen to 3.6 mgm. %, and clinically the jaundice diminished markedly but the cephalin flocculation was still strongly positive. The stool, which had shown no bile, became brown once more. By the tenth day of disease the urine had returned to normal. On November 22, bacteriological confirmation of the clinical diagnosis of Weil's disease was made. To prevent relapse, penicillin therapy was continued for three weeks, a total of 8,800,000 units being given. He received a total of 40 grams of streptomycin over a ten day period. The patient was discharged home on November 30, having spent twenty-three days in hospital. His convalescence was uneventful, and in spite of known hazards he has been carrying on at his old job ever since.

Bacteriology.—Numerous cultural examinations of eyes, throat, blood and sputum yielded no specific information. On the second hospital day, five days after the onset of illness,

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guinea pig inoculation with citrated whole blood was done as a diagnostic test for Weil's disease. Dark field examination of the patient's blood was not done. Ten days after inoculation, the guinea pig had a rise of temperature, followed in twenty-four hours by marked jaundice. Dark field examination of heart's blood at this time showed numerous highly active spirochætes. Attempts to culture the organism in Korthoff's medium were unsuccessful, but the disease was reproduced in guinea pigs by serial transfer of heart's blood at the time of temperature rise.

At postmortem, the animals showed marked jaundice and numerous petechiæ throughout the abdominal wall, peritoneum and viscera. There were many hæmorrhagic areas in the lung from 1 to 5 mm. in diameter, reproducing the classical picture of "butterfly lungs" associated with Weil's disease (Fig. 1). Sections

Fig. 1.—The "butterfly lung" petechiæ in the guinea pig.

of the organs were stained by Levaditi's method and examined for spirochætes. These were found in moderate numbers in the hæmorrhagic areas of the lung and liver, and in the lumina of the renal tubules.

Samples of serum, sent to the Laboratory of Hygiene, Kamloops, B.C. for agglutination tests, were negative up to the eighth day of illness but positive thereafter (Table I). The results of the complement fixation test parallel those of the agglutination tests as shown in Table I.

The diagnosis of Weil's disease in this instance was first entertained clinically because of the fact that the patient was a sewer worker, frequently in contact with rats and their excreta, who presented many of the characteristic features of the disease as outlined in the case history. Confirmation by the laboratory was based on (*a*) the reproduction of the disease in guinea pigs with the presence of spirochætes in the blood and tissues; (*b*) the successful transmission from one animal to another and (*c*) the strongly positive and adequately controlled serological tests.

DISCUSSION

Mode of infection.—Infection with *Leptospira icterohæmorrhagiæ,* in the majority of reported cases, is the result of contact with the excreta of rats. In the rat, this infection is a true epizootic. After a usually non-fatal septicæmia, the organisms settle in the distal convoluted tubules and are excreted in the urine for periods up to two years. Man is infected through the abraded skin, or the mucous membranes during contact with soil, water or fomites contaminated with rat urine. More rarely, Weil's disease results from a rat bite.[5]

The disease is becoming increasingly recognized as an occupational hazard, although not an occupational disease. In 1936, a fish worker in New York State was awarded compensation for leptospiral infection[9] and since April, 1940, it has been included in the schedule of industrial diseases under the Workmen's Compensation Act in Scotland and Wales.[10] The majority of cases have been in persons whose work is in wet places where rats are common, as in sewer workers,[11] tunnellers,[12], fishermen,[9, 13] miners,[10] slaughter house workers,[14] people who swim or fall into rat-infected water,[14, 15] and those who live or work in rat-infected quarters.[16, 17]

Estimates of the percentage of the rat population which are carriers of leptospira vary up to

TABLE I.

	Agglutination											*Complement fixation*							
Day of illness	*L. icterohæmorrhagiæ*							*L. canicola*				*L. icterohæmorrhagiæ*				*L. canicola*			
titres	*1:25*	*1:50*	*1:100*	*1:200*	*1:400*	*1:500*	*1:900*	*1:25*	*1:50*	*1:100*	*1:200*	*1:10*	*1:20*	*1:40*	*S.C.*	*1:10*	*1:20*	*1:40*	*S.C.*
5th	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
8th	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
14th	4+	4+	4+	4+	4+	4+	4+	–	–	–	–	3+	2+	1+	–	–	–	–	–
21st	–	4+	4+	4+	3+	2+	–	3+	1+	1+	±	4+	4+	4+	–	–	–	–	–
Pos. controls																			
L. ictero.	4+	4+	4+	4+								4+	4+	4+	–				
L. canicola								4+	4+	4+	4+					4+	4+	4+	–
Neg. control	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

40% depending on locality and on the age of the rats examined. Cameron and Irwin[18] demonstrated leptospira in 37% of 78 wild rats captured in Toronto and 69% of the 20 strains recovered were proved to be *L. icterohæmorrhagiæ*. If this incidence of infection among rats holds for the rest of Canada, it is rather surprising that a diagnosis of Weil's disease is not made more often.

Pathology.—The disease starts as a leptospiræmia so all organs are involved to a certain extent and show non-specific changes. There is an increased hæmolysis of the blood. Capillary fragility is increased due to the toxæmia, hence a hæmorrhagic diathesis is common. Epistaxis is frequent and hæmoptysis occasional, due to hæmorrhage in the lung. In the cases reported from Toronto, there was marked liver damage, with a disruption of the architecture and even necrosis of considerable areas. Van Theil,[5] in his monograph, states that liver damage is not usually extreme and is in sharp contrast to the extreme jaundice. Occasionally, however, death ensues due to a massive hepatic necrosis. The kidneys are always affected. There is albuminuria and hæmaturia which may go on to anuria. The main lesion is in the convoluted tubules where there is an interstitial mononuclear infiltration and degeneration of the tubules. The glomeruli are affected but little. Clinically the hæmaturia may suggest an acute glomerular nephritis, but is actually due to the hæmorrhagic diathesis. Leptospira are always found in the renal tubules and the interstitial tissue. The toxæmia and the vascular changes may affect the central nervous system, causing a variety of signs. Meningitis[19] is not uncommon and leptospira may be cultured from the cerebrospinal fluid. Cells, proteins and sugar may all be increased. Muscle fibres may show degeneration and there are no signs of repair until after the seventeenth day of the disease. The usual cause of death is uræmia which sets in after the patient is afebrile. The mortality from the cases reported in the U.S.A. is 30%.

Clinical course.—Inada[20] describes the disease as having three clinical phases. The incubation period varies between 4 and 12 days. In the first stage, septicæmia is present. This is the febrile phase, which is acute in onset. It lasts from 5 to 10 days and is characterized by fatigue, weakness and malaise. Headache is usually present and muscle pains may be pronounced, so much so that it may simulate an acute abdomen. Epistaxis, hæmoptysis and even gastro-intestinal bleeding may occur. There is marked hyperæmia of the conjunctiva and usually subconjunctival hæmorrhages. This, in conjunction with icteric scleræ, is almost pathognomonic of severe cases of leptospirosis.

The second stage is the icteric phase. The leptospira are no longer found in the blood but make their appearance in the urine. Occasionally this phase is abortive and the subsequent clinical course one of convalescence. The jaundice which appears in over 50% is of great intensity in severe cases. The liver may be enlarged and tender, the spleen rarely so. Hæmaturia is common and may go on to oliguria and even anuria. This is the commonest cause of death, resulting from the ensuing uræmia and vascular collapse. The signs of meningitis occasionally appear.

The final phase is that of convalescence. This is slow and great weakness is the main complaint. During this phase there may be another febrile attack and the whole course repeat itself.

Clinical diagnosis.—The paucity of cases in the literature of Canada, compared with that of other countries, would suggest that the diagnosis is seldom entertained. The acute onset of fever, prostration, muscle pains and injected yellow scleræ are important in anyone who may be exposed to rats. If there is no jaundice, the clinical picture is more difficult to recognize. Albumen and red cells are always present in the urine.

Laboratory diagnosis.—The final proof of the diagnosis of Weil's disease must come from the bacteriologist who has several diagnostic procedures at his disposal. All of these methods require close co-operation between clinician and laboratory.

1. *The agglutination test* is performed by the technique of Schüffner[21] using formalin-killed suspensions of spirochætes. Circulating antibodies appear in the blood from the ninth day on. A titre of 1:300 is considered diagnostic, particularly when the titre rises on successive samples. It may rise to 1:100,000 and persists at high levels from one to twenty years,[22] so that diagnosis may be made in retrospect.[23] Many workers[5] prefer to use living suspensions of leptospira as the antigen in the test, since

there is less likelihood of auto-agglutination. However, this method is not convenient for most hospital laboratories.

2. *The complement fixation test*[5] is a useful method for small laboratories where the serological diagnosis of Weil's disease is requested only occasionally and where cultures are not readily available. Formalin-killed antigen may be stored for several weeks.

3. *Guinea pig inoculation of blood or urine* as a means of diagnosis is second in importance to the serological methods. Leptospira can be found in the patient's blood only during the first week of illness, preferably the 3rd to 5th days, and in the urine only after the 7th day. This method has many pitfalls,[24] but where successful, is absolutely reliable. Within 10 to 14 days, the animal shows a marked rise in temperature, at which time spirochætes can be demonstrated in the blood by dark field examination. Within a few hours of the temperature rise, jaundice appears and the animal dies of leptospiræmia in another 4 to 5 days. At postmortem, all tissues are jaundiced. There are usually many petechiæ, which, in the lung, give the appearance described as "butterfly lung". With Levaditi's stain spirochætes in liver, lung and kidney can be demonstrated.

4. *The mouse protection test* devised by Larson[25] is specific for Weil's disease. It is based on the fact that in the patient protective antibodies develop during the second week of illness and persist for at least five years. Mice are injected with mixtures of infective material and serial dilutions of patient's serum. The degree of protection afforded the mice is estimated. The mouse protection titre roughly parallels the agglutination titre.

5. *Darkfield examination* of patient's blood as a diagnostic test is not considered too reliable owing to the presence of pseudo-spirochætes.[26]

6. *Culture from patient's blood* is not practicable in a small laboratory or in many large ones due to the special media required.

THERAPY

Prior to the antibiotic era, the treatment of choice was convalescent (immune) serum.[12] However this was difficult to obtain and the effects were rather uncertain. In 1944, Heilman and Herrel[27] reported good results with the use of penicillin in experimental infections in guinea pigs. Augustine, Weinman and McAllister[28] concluded that in guinea pigs, penicillin has a suppressive action if given before the appearance of symptoms, but that it is not curative. Larson and Griffiths,[29] comparing the action of immune serum and penicillin in infections in mice, found them equally efficacious up to 48 hours though much less active beyond 48 hours. Patterson[30] described three human cases treated with immune serum and six others with penicillin, in a dosage of 15,000 units every three hours, both of which were effective. Bulmer[31] used 40,000 units every three hours in treating 16 British soldiers with Weil's disease, and concluded that the drug produced clinical improvement in 36 hours with a reduction in fever and the number of relapses. Cross[32] and Liebowitz[8] have each treated one case successfully with penicillin. Heilman has studied the effect of streptomycin[33] and aureomycin[34] against experimental leptospiral infections in guinea pigs using equivalent weights. He found streptomycin less effective and aureomycin twice as effective as penicillin. There have been no clinical reports on the use of either of these antibiotics in human cases as yet.

In the case just reported, the effect of streptomycin cannot be determined adequately since the patient received penicillin as well. The beginning of a favourable response appeared to antedate the exhibition of streptomycin.

SUMMARY

1. A case of Weil's disease (*Leptospirosis icterohæmorrhagica*) has been reported which was treated with penicillin and streptomycin and recovered: this is the first such case in the Canadian literature. Two fatal cases have been reported from Toronto.

2. The mode of infection, clinical course, diagnosis and treatment of this disease are discussed.

Our thanks are due to Dr. F. A. Humphreys, bacteriologist in charge of the Kamloops, B.C. Laboratory of Hygiene, Department of National Health and Welfare, for performing the serological tests.

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IMMOBILIZATION OF TREPONEMA PALLIDUM IN VITRO BY A SPECIFIC ANTIBODY PRODUCED IN SYPHILIS AND COMPLEMENT

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IN Dr. Turner's laboratory, at the Johns Hopkins School of Hygiene, Drs. Robert A. Nelson, Jr. and Manfred M. Mayer have developed techniques which make it possible to demonstrate the presence of a true syphilitic antibody in the serum of human beings and animals infected with treponema pallidum. This antibody, acting in conjunction with fresh guinea pig complement, produces immobilization of virulent treponemes *in vitro*.

A prerequisite for the immobilization test is the preparation of treponeme suspensions in a special media (Nelson's) which keeps the *Spirochæta pallida* alive for 8 days, with retention of motility and virulence; the movements are even more rapid than those of spirochætes collected from human lesions.

Preparation of treponema suspensions. — The *Spirochæta pallida* do not multiply in the media; therefore, as yet, their culture is not possible *in vitro*. A fresh supply must be assured by inoculating rabbits, twice a week, with organisms extracted from rabbit testicular syphilomas.

Source animals are injected deeply into each testicle with two ½ c.c. doses of a freshly prepared suspension of treponemes. They are examined daily for the development of orchitis, which usually appears about the seventh day. It is of primary importance to kill the animals no later than 24 hours after orchitis develops, otherwise antibodies may be produced in the host itself which would interfere with the reactions. If no lesion occurs within 14 days the inoculation is considered unsuccessful and the animal discarded.

Animals developing orchitis are bled from the heart and killed by air injection. Their scrota are removed, aseptically opened with blade and scissors, the testes removed, washed with saline and cut into 10 slices with a specially constructed instrument. Further cutting will increase the contact surface of the syphilomas with the media during the process of extraction.

For the extraction, all portions from two testicles, after being washed with chilled 0.85% saline, are placed in 40 c.c. of Nelson's medium in a 250 c.c. flask, under an atmosphere of 5% carbon dioxide and 95% nitrogen, and rocked gently for two hours at 35° C. (water bath). Enumerations of the treponemes are made after one and two hours. The optimum numbers of 10 millions organisms per c.mm. should not be exceeded. Higher counts should be reduced by adding sufficient volume of the basal medium. The treponemes are separated from the testicular debris by centrifugation at 1,000 r.p.m. for 10 minutes at room temperature. The crystal clear supernate contains the treponemes and is used in the test.

Test procedure.—The human serum to be tested, the fresh guinea pig serum and the suspension of treponemes are pipetted into 13 x 100 mm. pyrex Wassermann tubes: one for the reaction, one for the control. In the latter, the guinea pig serum is deprived of its complement by inactivation at 56° C. for 50 minutes. The serum to be examined must also be inactivated for 30 minutes.

	Test	*Control*
Serum to be examined, inactivated	0.05 c.c.	0.05 c.c.
Guinea pig serum, containing complement	0.05 c.c.	
Guinea pig serum inactivated		0.05 c.c.
Suspension of treponemes (antigen)	0.4 c.c.	0.4 c.c.

Loose cotton plugs are placed in each tube; all tubes are incubated 18 hours at 35° C. in a Brewer anaerobic jar filled with a gas mixture of 5% carbon dioxide and 95% nitrogen.

These experimental conditions assure optimum survival of the treponemes. All manipulations should be done aseptically and as rapidly as possible. For this reason, counting of the organisms, at the end of the incubation period, may be limited to 50.

READING THE RESULTS: CRITERIA FOR ABNORMALITY

The mean percentage of active organisms reads as follows:

Control.—Serum from syphilitic or normal person plus heated complement: 89% active

organisms. If less than 70% organisms are motile, the test is considered as unsatisfactory.

Test.—Normal serum plus active complement: 85% active organisms. Syphilitic serum plus active complement: 4% active organisms.

The test is considered positive, if the percentage of motile organisms in the test tube is at least 50% below that of the control tube. Less than 20% difference between the number of active organisms in the control and the test tubes is considered a negative result.

In all tests which fail to show immobilization, there must be free complement present at the end of the 18 hrs. test period; its presence must be checked by adding sensitized sheep erythrocytes. If no hæmolysis occurs, the negative test is not considered valid and must be repeated.

Specific properties of the immobilizing antibody.—The immobilization of *Treponema pallidum* by the syphilitic antibody occurs only when complement is added to the mixture. Further proof of the interaction of the antigen, the complement and the specific antibody is furnished *in vitro* by the treponemes losing their virulence during the incubation of the mixture.

Specificity of the immobilization test has been clinically demonstrated by Nelson and associates at the Johns Hopkins Hospital, also by Harold J. Magnuson at the University of North Carolina. No positive immobilization test has been encountered in non-syphilitic individuals, even those with positive standard serologic tests for syphilis due to atypical pneumonia, varicella or infectious mononucleosis. In syphilitic patients the immobilizing antibody is found to develop relatively early in the course of the disease, to be constantly associated with secondaries, and to remain at a high level in late latent syphilis. A small group of patients with untreated late syphilis whose sera failed to react with standard serological tests were found to give strongly positive immobilization tests.

Reagin Found by Serologic Tests for Syphilis and Immobilizing Antibody

These are two different entities, as has been demonstrated by absorption experiments. A syphilitic serum may have its reagins removed by flocculation with Kahn, Eagle, or another non-specific antigen, and still retain its immobilizing action against treponemes in presence of complement. Further evidence that the immobilizing antibody is distinct from reagin will be found following treatment of cases of late syphilis; although the reagin titre declines, the immobilizing antibody is apt to remain at a constant level.

Relationship between immobilizing antibody and immunity.—Such a relationship is sufficiently demonstrated, since the antibody acting with complement kills treponemes *in vitro;* also by the fact that, in experimental syphilis, the development of resistance to infection, which means immunity, rather closely parallels the level of immobilizing antibodies, as revealed by quantitative tests.

Value of the immobilization test for treponema pallidum.—The immobilization test offers a convenient approach to the study of fundamental problems in the biology and immunology of syphilis in animals and human beings (Nelson). The test also may be of value in differentiating a biologic false positive reaction from positive serologic results due to syphilis in patients who have neither evidence of the disease nor history of infection. In 20 cases of proved false positive serologic tests, treponema immobilizing tests were negative.

More extensive clinical application of the immobilization test awaits cultivation of treponemes *in vitro.* This test may still be five years away from practical usefulness for the diagnosis of syphilis (J. Mahoney).

As a result of my visit in January last to Dr. Turner's laboratory, where I have seen the test being performed and read its results, and had the privilege of spending hours with Dr. Nelson, I am convinced that the immobilization test deserves to be well known by syphilologists and practised in research laboratories.

Summary

1. Dr. Nelson has demonstrated the presence, in the serum of syphilitic persons and animals, of a specific immobilizing antibody for *Treponema pallidum.*

2. By the combined action, *in vitro,* of this antibody and complement, *Treponema pallidum* loses not only its motility but also its virulence. Direct relationship between the titre of this antibody and immunity to new infection is established by experimental syphilis.

3. The immobilizing antibody is distinct from the reagin found by serologic tests for syphilis. Its titre remains constant after treatment in latent syphilis, while the reagin level usually declines.

4. Practically all sera from patients with syphilis, beyond the primary stage, give positive immobilization tests. No positive result has been obtained with sera from normal individuals or from patients with diseases other than syphilis.

5. The immobilization test is at present inapplicable for the general diagnosis of syphilis. However, its high degree of specificity suggests its possible use for differentiating biologic false positive results from true positive serologic reactions in latent syphilis.

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ACUTE ABDOMINAL PAIN AND SHOCK ASSOCIATED WITH HÆMOCHROMATOSIS*

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THE most significant pathological lesions in hæmochromatosis are found in the liver and pancreas, both of which organs show a heavy deposit of iron pigment with fibrotic changes. In the later stages and probably associated with the pancreatic lesions there frequently develops a diabetes mellitus and this, if associated with skin pigmentation, results in the classical textbook picture of "bronzed diabetes".

One does not usually associate abdominal pain as a prominent symptom of this disease though Sheldon[1] in his monograph states that 6% of cases showed it at some time in their history. More recently Desforges[2] found that abdominal pain was a prominent feature of the clinical course in six patients out of a total of 40 proved cases of hæmochromatosis seen at the Boston City Hospital, in a ten year period. Of these six cases, three had demonstrable causes for the abdominal pain; one had liver failure; one had a hepatoma and one had a ruptured diverticulum with peritonitis. The remaining three cases had no morphologic background as a basis for the bizarre abdominal symptomatology, in two of which there was also associated shock; the only demonstrable pathological lesion being hæmochromatosis involving various organs, notably the liver, kidneys, pancreas and heart.

Hurxthal[3] reported a case of hæmochromatosis in which abdominal cramps and diarrhœa had been noted before admission while Boland and Curran[4] have reported two interesting cases occurring in brothers, one of whom first presented with signs and symptoms resembling cholecystitis for which a cholecystectomy was performed; the gall bladder proved to be normal on pathological examination but the liver was brown and cirrhotic. A diagnosis of hæmochromatosis was confirmed and he died nine days postoperative in hepatic coma. Later his brother developed similar symptoms, a diagnosis of hæmochromatosis was made by skin biopsy, operation was therefore not done and he recovered with general medical care.

Such reports dealing with abdominal pain as a symptom of hæmochromatosis appear to be very few, at least in the English medical literature. However, Desforges[2] quotes Boulin[5] as stating that in 70 cases of hæmochromatosis studied, 34% of the patients were originally admitted to hospital because of painful abdominal crises, those located in the gall bladder region being especially severe.

Because such a symptom occurring in hæmochromatosis does not appear to be generally known, it was felt that the following case was worthy of presentation, more particularly since shock was an outstanding feature, and recent work on the metabolism of iron offers an intriguing theory as to its relationship to hæmochromatosis.

CASE REPORT

A 51-year old white male was admitted to hospital on March 22, 1950, and died the following day. For 9 hours before admission he had severe, crampy, stabbing pain all over the lower abdomen with pain through to the sacrum. This pain was of sudden onset. Two hours after the onset, he vomited once. He had had no bowel movement since the pain began. There was no history of previous gastro-intestinal upset, ulcer or dyspepsia and he claimed to have been perfectly well previously. Past history was not significant. At the time of admission to hospital, the patient was in pain so great that he was unable to complete the necessary records.

Physical examination by the intern showed a well developed, middle-aged man who was pale, breathing rapidly, but not perspiring. Ear, nose and throat examination was negative. The lungs were clear to percussion and auscultation. Heart sounds were faint but apparently normal. Blood pressure 95/60, pulse 80 and regular, of fairly good volume. The abdomen showed

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board-like rigidity throughout and on palpation he complained of a generalized acute tenderness which seemed least in the costo-vertebral angles posteriorly. There was no tenderness over the sacrum but he complained of an increase of pain on extending his limbs. He refused to blow up his abdomen or take a deep breath because of the pain. Rebound tenderness was present on both sides. The patient preferred to lie in a semi-flexed position. The remainder of the physical examination was non-contributory.

Following a barium enema, radiologic examination revealed half the barium remaining in the large bowel, which was dilated and fluid levels were visible subsequent to the enema. No evidence of free gas was detected in the peritoneal cavity. The rectum appeared somewhat narrower than usual but showed no constant deformity.

Laboratory reports were as follows: Urinalysis—Reaction pH 6.0, specific gravity 1.025, occasional white cells, epithelial cells and hyaline casts, otherwise negative. Urine urobilinogen was 2.08 mgm. per 100 ml. (Normal 0.8 mgm. per 100 ml.). Bile salts were present and there was a trace of bile pigments. Blood diastase was 6 units, (normal 4 to 16). Urinary diastase was 6 units, (normal 8 to 32). White blood cell count was 6,800 per c.mm. with a differential count of polymorphonuclears 22%, staff 64%, myelocytes 2%, lymphocytes 5%, monocytes 6%, eosinophils 1%.

The patient appeared to be in shock and a tentative diagnosis of acute pancreatitis was considered. However, since perforation of a viscus could not be definitely ruled out, it was felt that laparotomy was indicated. Morphine gr. 1/6 and atropine gr. 1/100 were given one hour before the operation, which was done under spinal anæsthetic using pontocaine 10% in glucose with ephedrin gr. 1½. Oxygen was administered by mask as required and curare 2 c.c. was given intravenously one hour and twenty minutes after commencement of the anæsthetic; 5% dextrose in water was administered intravenously throughout the operation.

On opening the peritoneum, the coils of small intestine seemed somewhat more moist than usual and a sterile swab was inserted between them for smear and culture. Subsequently this gave a light growth of *B. coli*. About 2 ounces of salmon-pink coloured, thin fluid lay in the pelvic cavity and this was removed. There was no evidence of peritonitis. The pancreas and gall bladder were palpated and seemed normal in size and shape. The appendix was normal. Inspection and palpation of the abdominal organs revealed no abnormality other than an increased bogginess in the retroperitoneal tissues. The abdomen was therefore closed without further procedure, two hours after commencement of anæsthesia. At this time the patient's blood pressure was 90/60, pulse 100, irregular and poor. Oxygen was administered by mask and tracheal suction used as necessary. The patient remained somewhat cyanosed. Two hours later, the pulse was still rapid and shallow with a rate of over 130. Temperature rose to 103.4, respirations were 58 per minute. Considerable sero-sanguinous drainage from an inserted drainage tube was reported. Seventeen hours after operation the patient showed Cheyne-Stokes breathing, was confused and restless, complaining of abdominal pain. Nineteen hours after operation, blood pressure was 76/40, pulse more than 130, respirations 48, colour poor and the patient very confused. He died two hours later.

Autopsy findings.—The body was that of a middle aged white male, about 5 feet, 10 inches in length, of good development and slightly obese. The thyroid was not palpable. No enlarged glands were found and there was no pigmentation of the skin.

Lungs.—The right weighed 840 gm. and the left 570 gm. Both were voluminous, moderately heavy and showed acute congestion with some pulmonary œdema. The pleural cavities were dry.

Pericardial cavity.—There were a few fine petechial hæmorrhages scattered over the left auricle and ventricle posteriorly. The *heart* weighed 420 gm. and showed mild hypertrophy of the left ventricle but otherwise appeared normal, the coronary vessels were mildly atherosclerotic and widely patent throughout.

Peritoneal cavity.—A lower midline abdominal incision of recent origin was noted and the area around the operative site showed mild hæmorrhage, with some thickening of the adjacent tissues. About 30 c.c. of salmon coloured fluid was found in the pelvic cavity. There was marked œdema of peri-renal tissues on both sides, especially on the right. The peritoneum, both visceral and parietal, was glistening and showed no evidence of acute peritonitis or fat necrosis. *The gastro-intestinal tract* was carefully examined throughout and no significant gross disease was found. In particular there was no perforation or ulceration. The stomach mucosa was bile stained and the rectum contained some barium. The *liver* was large, weighing 2,200 gm. The surface was brown in colour and firm. The cut surface showed a fine nodular pattern suggesting a fine cirrhosis. A portion gave an intense Prussion blue reaction for hæmosiderin when tested. The gall bladder was large, full of green bile and no calculi were found. The cystic, hepatic and common bile ducts were dissected out carefully and showed no obstruction or perforation. The lymph glands in the porta hepatis were soft, enlarged and a dark greenish-brown colour externally, their cut surfaces being of similar colour; a portion of one gave an intense Prussian blue reaction. The *pancreas* was normal in size and shape but rather firm on palpation. The external surface showed a peculiar greenish mottling and transverse section showed a uniform light brown colour. No areas of fat necrosis were seen. The main pancreatic duct had an opening in the ampulla of Vater 2 mm. from the opening of the common bile duct. No obstruction was demonstrable in its lumen and there was no evidence of bile staining. A portion of pancreas gave a moderate reaction for hæmosiderin. The *adrenals* were normal in size and shape but showed the same peculiar greenish mottling of the surface as seen in the pancreas. The cut surface showed the usual brown colour of cortex with a pearly grey medulla. The *spleen* weighed 240 gm. The external surface appeared normal and the cut surface showed a dark mottling suggesting petechial hæmorrhages. A portion gave a positive reaction for hæmosiderin. The *kidneys* appeared normal externally and on cut surface, except for some congestion. The bladder, prostate and urethra were normal. There was moderate atherosclerotic change in the intima of the aorta. The *brain* was not examined.

Microscopic examination.—H. and E. and Prussian blue stains were performed on all blocks of tissue. The *liver* showed a moderate fibrosis in the portal areas with thin strands sweeping into the liver parenchyma. There was no bile duct proliferation nor inflammatory cell reaction. All sections showed a tremendous deposition of brown pigment granules, giving an intense Prussian blue reaction. This pigment was found in all types of cells, liver cells, reticulo-endothelial cells and also in the cells of the cholangioles in the portal tract.

The *lymph glands in the porta hepatis* showed dilated sinusoids in which were numerous macrophages packed with hæmosiderin granules. The *pancreas* showed moderate hæmosiderin deposits in the alveolar cells and to a lesser extent in the cells of the islets of Langerhan. There was however no fibrosis. No areas of fat necrosis nor acute inflammatory change were seen in many blocks examined. The *spleen* was intensely congested and moderate numbers of macrophages in the sinusoids contained hæmosiderin granules. In the *adrenals* a few hæmosiderin granules were scattered throughout the cortex and in the cells of the medulla; no other pathological lesions were seen.

The *skin* appeared normal. No hæmosiderin deposits were seen. Sections from the *parathyroid, prostate* and *stomach* revealed occasional cells filled with hæmosiderin granules while the thyroid, lungs and heart showed no evidence of hæmosiderosis there only being congestion and œdema in the lungs and a few small focal areas of fibrosis in the heart.

Numerous sections were taken of the *peritoneum, retro-pancreatic tissues, retroperitoneal tissues* and from

various parts of the abdominal cavity. There was no evidence of peritonitis in any of these sections and the only positive finding was the presence of a few polymorphonuclears and lymphocytes in one section of fatty tissue near the pancreas, but this was not of sufficient intensity to denote more than a minimal degree of inflammation. It was therefore felt that the scant growth of *B. coli* obtained at the laparotomy was in all probability merely a contamination since no evidence of infection was found at autopsy.

The final pathological diagnoses were: hæmochromatosis involving liver, pancreas, spleen, lymph nodes of porta hepatis, stomach, and adrenal; portal cirrhosis of liver, moderate; retroperitoneal œdema.

Three other cases of hæmochromatosis were found in the records available. In two of these cases there were episodes of abdominal pain, in one of these autopsy showed the usual findings of hæmochromatosis with no morphological grounds to explain the pain. The other case was admitted because of peri-umbilical pain of short duration; hæmochromatosis was diagnosed by skin biopsy but this patient was lost sight of.

Discussion

The two outstanding features noted in the clinical condition of this patient were the abdominal pain and prolonged shock; his blood pressure on admission was 95/60, during the exploratory laparotomy it was 90/60, falling to 76/40 two hours before his death. Recent work dealing with iron metabolism offers a tempting explanation for the association of the shock with the morphologic findings of hæmochromatosis, but no sound explanation can be given for the symptom of abdominal pain.

Granick[6] in a very informative paper on iron metabolism points out that iron is normally stored in the body as an invisible compound called ferritin which is a combination of ferric hydroxide with a protein apoferritin. He postulates that hæmochromatosis is a metabolic disease in which there is probably increased absorption of iron through the mucosa of the intestine, in particular the duodenum, where normally the lining cells act as a regulating mechanism governing the absorption of the iron as required by the body. He further suggests that the metabolic error in hæmochromatosis may be due to a slightly greater reducing tendency of the mucosal cell for iron with consequent increased absorption of the ferrous ion and that this increased reduction may be related to an increased effectiveness of reducing enzymes, or by a decreased efficiency of oxidizing enzymes. In any event the body stores of ferritin become saturated and it is believed that the excess ferritin molecules then become linked to form a visible iron pigment called hæmosiderin.

Recently Mazur and Shorr[7] have proved that ferritin is identical with their so-called vasodilator material (VDM) of hepatic origin, which Shorr and his co-workers[8] had previously demonstrated to be present in the blood of experimentally shocked animals and which together with its antagonist, the vaso-excitor material (VEM) of renal origin, is receiving much attention in studies dealing with the pathogenesis of shock and essential hypertension.

Thus in hæmochromatosis the liver not only contains an excess of hæmosiderin, but also an excess of ferritin which is a vaso-depressor material proved to be in the circulation during the stage of irreversible shock. One is therefore tempted to postulate that the severe irreversible shock which was the cause of death in the patient under discussion, might well have resulted from release of ferritin into the blood stream, a complication suggested as a possibility by Granick.[6] It should be noted that in the three cases of hæmochromatosis reported by Desforges,[2] two of the patients showed a shock-like picture with peripheral vascular collapse in addition to abdominal pain, while the third patient showed signs of progressive cardiac decompensation.

The abdominal pain which was the presenting symptom of this patient is much more difficult to explain. No pathological lesion other than œdema of the retroperitoneal tissues and mesentery was found which, in our present state of knowledge, could be correlated with the pain. It is possible that this œdema was related to the vaso-dilatation which we are postulating as the pathogenesis of the shock.

Adrenal cortical insufficiency and liver failure are two other hypotheses that have been offered[2] as explanations for the abdominal pain. In the present instance there is no direct evidence that either of these conditions pertained, neither can we rule them out since no functional tests were done. Certainly it is not uncommon to see epigastric pain as a symptom of liver disease such as cirrhosis or hepatic necrosis but the severity of the pain seen in this case appeared to be greater than that associated with such lesions.

Summary

A case of hæmochromatosis has been presented in which the predominating symptoms

were acute abdominal pain and shock, the latter being the cause of death. The only morphological findings at autopsy were those of hæmochromatosis. The literature dealing with acute abdominal pain as a symptom of hæmochromatosis has been briefly reviewed.

From the recent literature dealing with iron metabolism and the pathogenesis of hæmochromatosis, it is suggested that the irreversible shock seen in this patient was possibly due to a release of the iron storage product ferritin which has been shown to be identical with the vaso-depressor substance (VDM) of Shorr and his co-workers.

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NEUROFIBROSARCOMA OF THE OVARY, ASSOCIATED WITH NEUROFIBROMATOSIS

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NEUROFIBROMATOSIS (Von Recklinghausen's disease) is a familial condition and is characterized by nodules of the skin of varying size from that of a small pea to an egg and associated with light or dark brown pigmentation. The lesions are said to originate usually in the sheaths of Schwann of the fine cutaneous nerves (see Fig. 1). They may, however, occur in the cranial nerves, deeper and visceral nerves. Boyd states that the deeper growths are prone to malignant or sarcomatous change and frequently cause death. Charachie of Brooklyn states that the general tendency to excise symptomless neurofibromata for diagnosis or therapeutic purposes, should be condemned, especially those not increasing in size and not exposed to irritation. Such procedures, instead of preventing a small innocent fibroma from developing into "cancer", stimulate it to undergo sarcomatous change. This has been found to occur in about 12% of cases.

Neurogenic sarcomas are radio-resistant. Once sarcoma has developed one must do radical surgery. Their innocent appearance and accessibility to removal provide an inviting setting for a simple excision. Pulmonary metastases frequently occur. The primary excision must be radical. Multiple neurofibromatosis like leucoplakia deserves watching. Neurogenic sarcoma is rarely diagnosed prior to operation or biopsy. In the presence of neurofibromatosis a clue is presented. A search of literature does not reveal the reported occurrence of any neurofibrosarcoma of the ovary associated with fibromatosis. I wish to present the following case of neurofibrosarcoma of the ovary associated with Von Recklinghausen's disease.

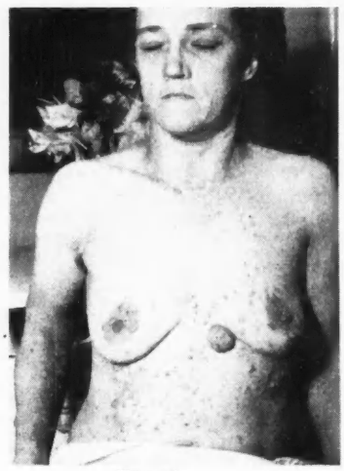

Fig. 1

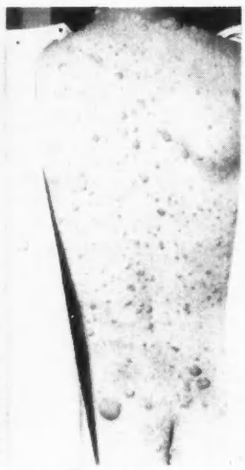

Fig. 2

CASE REPORT

Mrs. A.G., aged 38, was admitted to the Ottawa Civic Hospital September 21, 1948, complaining of vaginal bleeding. The bleeding had begun eight days prior to admission and was only slight at first. Six days before admission she had a profuse hæmorrhage and believed that the products of pregnancy were extruded. She had been bleeding moderately until about four days prior to admission, when the bleeding slowed considerably. She had no pain. She had menstruated 21 days with 7 days' duration with a moderate flow, backache, and her last menstrual period was on June 5, 1948. There was only moderate leukorrhœa. She had had seven pregnancies and five full-term live children, the last 3½ years prior to admission to hospital. This she claimed was her second spontaneous abortion. She had no urinary disturbances and her gastro-intestinal system was normal. She stated that her mother suffered from "lumps" on her skin very similar to those which she herself had.

She was fairly well-nourished, with patchy, café-au-lait pigmentation of her body, with thousands of varying sized nodules from the size of a pin to that of a walnut scattered over the whole body, including the face. Her temperature was 101.2°, pulse 100, respirations 20. Her heart and lungs were normal, blood pressure 122/84. Her abdomen revealed two distinct non-tender, very well-fixed masses, each the size of a large orange, one in the right upper and one in the right lower quadrant. The upper mass seemed fixed medially but could be moved laterally. Pelvic examination revealed a mass the size

of an olive in the left vaginal wall which was considered to be a fibroma. There was a stellate laceration of the cervix and the cervical os was less than one finger and was firm. The uterus was about two-months' size. There was a mass to the right and beyond the uterus; fairly firm, about the size of a large orange and feeling like a solid ovarian cyst. There were a number of neurofibromata over the vulva as well as the vaginal mucosa.

The urine showed very faint trace of albumin, sugar none, a few white blood cells and epithelial cells. Red blood count was 3,400,000, white blood count 8,350, Hgb. 11.1 gm. or 70%. Sedimentation 57 mm. in one hour. Blood sugar 105 mgm. % and the non-protein nitrogen 29 mgm. %. Blood Wassermann was negative. X-ray of the chest showed no evidence of metastases. The lung fields were clear. The heart and aortic shadows were normal. There was no abnormality about the bony detail of the lumbar spine and pelvis. She was Rh positive.

In view of her history it was assumed that she had suffered an abortion; the diagnosis was also made of neurofibromata of the vagina, vulva, the abdominal wall and pelvis, as well as neurofibromata of the skin (Von Recklinghausen's disease).

On September 21, she was given penicillin 100,000 units every 4 hours, and two days later, when her temperature was normal, she was taken to the operating room and a D. and C. was performed. At operation

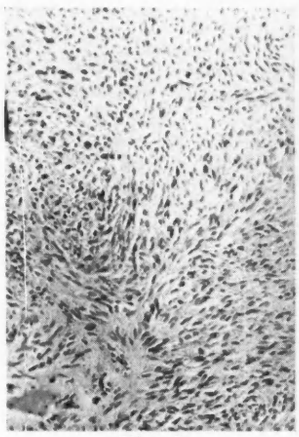

Fig. 3

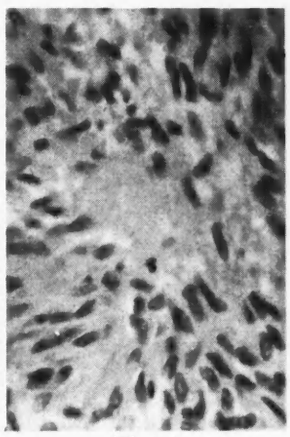

Fig. 4

several strands of white, soft endometrial tissue with some blood clot was obtained. Microscopic examination of this tissue showed the presence of acute endometritis and decidual mucosa with acute inflammation. No chorionic villi were encountered.

A week later, she was taken to the operating room for removal of the pelvic mass. A large, fairly firm orange-sized bluish cyst was found. This bled on the slightest touch. The small bowel loops were densely adherent and the appendix was also attached to the mass. The sigmoid was also attached to the tumour and was extremely friable. As much as possible was resected and the bowel serosa was sutured with catgut where the adhesions were removed. Bleeding was controlled with sutures. Where the tumour invaded the sigmoid it was not found possible to resect it, for the mass was intra-luminal as well as extra-luminal. Bleeding was controlled and the cyst-like tumour was traced back to the right ovarian pedicle. The left ovary was found to be normal but a yellow, solid, lipoma-like mass was taken out of the left broad ligament. The mass in the right upper quadrant was palpated and was found to be an intra-mural neurofibroma. Several others were palpated extra-peritoneally in the abdominal wall. The appendix was removed in the usual manner. The patient was discharged on October 19, in good condition and was referred to the tumour clinic for further observation.

Pathological report (Dr. M. O. Klotz).—The appendix showed evidence of inflammatory changes, with some peri-appendicitis. Accompanying the appendix was a small oval-shaped mass of tissue which apparently was the small tumour removed from the left broad ligament. This measured 3 cm. in length, 2 cm. in breadth and 1 cm. in thickness. It was rounded and even in contour and pale yellowish white in colour. On section the cut surface was firm but jelly-like and translucent in appearance. It was uniformly well encapsulated. Its central core was somewhat fibrous and appeared to be slightly calcified.

Also received were a large number of fragments of varying sizes of firm and irregular tissue which was accompanied by a large portion of blood clot. The largest portion of tissue measured 7 cm. in length, 2 cm. in breadth and 1.5 cm. in thickness. These were accompanied by a small flattened portion of tissue which had been removed and used for quick section. On gross examination these fragments of tissue had a flattened appearance suggesting that they had been portions of the wall of a cyst-like structure. Each fragment had one surface covered by a thin capsule roughly bluish-grey in colour with nodular white areas here and there. In some portions the surface was very markedly nodularly irregular and what appeared to be the inner surface was, in all fragments, rough and irregular in appearance, and coated with varying amounts of clotted blood. On section this tissue was firm but very friable and rather white and translucent in appearance. Attached to one fragment was a portion of a Fallopian tube which measured 4 cm. in length, and was covered with thin, smooth and glistening serosa. Its fimbriated end was patent and on section the mucous membrane was soft, pale and filiform in appearance. No definite ovarian tissue could be demonstrated.

Sections of the large ovarian tumour showed this lesion to be of a rather interesting nature. The growth was composed characteristically of elongated cells with a moderate amount of cytoplasm and attenuated ovoid nucleus. These cells tended to be arranged in parallel vesicular strands and in some instances whorls. They were separated from one another by a small amount of delicate, acidophilic, fibrillar material. Here and there the nuclei showed a definite tendency to assume a palisade arrangement such as is seen in lesions of neurogenic origin. Moderate numbers of well formed vascular channels were present throughout the growth, while here and there localized hæmorrhages were to be seen. For the most part the tumour cells were fairly uniform in all their characteristics though in some areas the growth was excessively cellular with an associated disappearance in the intercellular fibrillar material. Here it was noted that many of the tumour cells tended to assume a radial form about the smaller blood vessels. In these areas of increased cellularity, the constituent cells varied moderately in their size, shape and staining characteristics, some definitely typical forms being demonstrable. Despite this, no actual mitotic figures were encountered.

A small tumour removed from the opposite broad ligament was composed of a myxomatous, loosely arranged fibrous material of a relatively acellular character and showing little resemblance to the large growth present on the opposite side. This lesion appeared to be well limited by a delicate fibrous capsule. Other sections of the appendix showed the lumen to contain a small amount of debris, while the lining mucosa, though intact, was of a regenerated type. All coats of the appendiceal wall were thickened, œdematous, while the serosa was involved in an active inflammatory process characterized by a moderate infiltration of polymorphonuclear leukocytes which was associated with extreme œdema, hyperæmia and some fibroblastic response.

Diagnosis.—(1) Neuro-fibrosarcoma of ovary (right). (2) Neuro-fibroma of broad ligament (left). (3) Acute peri-appendicitis.

Subsequent course.—The patient, from October 12 to November 22, 1948, was given 20 deep x-ray treatments with a total of 6,240 R. At the time of her first treatment her weight was

111¾ lb. Though these tumours are known to be radio-resistant, it was thought that nothing would be lost by giving her this course of deep x-ray therapy.

She last reported on September 2, 1949, weighing 129 pounds, having gained 18 pounds since the preceding November. She looked well. Beyond a moderate leucorrhœa there was no complaint. The neurofibromatosis was unchanged. Pelvic examination showed a red cervix which was displaced to the left. There were no vault abnormalities. There were no changes in the mucosa of the cervix. Pelvic examination revealed no bleeding, and a moderate whitish leucorrhœa. The uterus and adnexal regions appeared clear. She was ordered to return for a re-check in March, 1950.

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CASE REPORTS

SUBLINGUAL DERMOID CYST

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The following case-report presents the typical history, clinical, operative and pathological findings of a sublingual dermoid cyst. This is a relatively uncommon lesion and for that reason this presentation is thought worth while.

Mrs. M., a 23-year old woman was first seen on March 7, 1950, complaining of a swelling beneath her chin and tongue and increasing difficulty in articulation. At five years of age, her mother had taken her to a doctor because of a swelling beneath her chin. The doctor did not advise treatment at that time. The swelling became less obvious and she "paid no attention to it" until the fall of 1948. At this time she began to notice a double chin and some difficulty in pronouncing certain words. The swelling was quite obvious beneath her tongue but caused her very little inconvenience. However, during the latter part of 1949 she noticed a progressive enlargement of the swelling, with increasing speech difficulty and the lump had become so large that she was unable to brush her molar teeth. The remainder of the history was irrelevant.

Examination disclosed an obvious mid-line submental swelling (Fig. 1) and when she opened her mouth there was a large mid-line sublingual swelling, with the tip of her tongue peeking over the top of the tumour. On closer inspection of the sublingual region, one noticed the sublingual folds stretched over the lateral aspects of the swelling and in the mid-line there was a definite yellowish-white coloration. Sublingual-submental palpation disclosed a peculiar doughy, fluctuant sensation to the examining fingers. There was no palpable abnormality of either the sublingual or the submandibular glands and no cervical lymphadenopathy. An index finger could be passed over the dorsum of the tongue to the region of the foramen cæcum and careful palpation in this region revealed no abnormality. The isthmus of the thyroid gland was barely palpable in the normal location.

A needle was inserted into the submental aspect of the swelling and 1 c.c. of thick, greyish, grumous material containing numerous fine yellow granules was aspirated. Under the microscope these fine granules were seen to consist of clumps of cholesterol crystals.

On March 21, the patient was operated upon under general anæsthesia, a Magill tube being inserted via the nasal route. The submental region was entered through a transverse incision, the fibres of the platysma and mylohyoid muscles being divided in the direction of the incision. The tumour mass was found lying immediately above the mylohyoid muscle. It was well encapsulated, the capsule being yellowish-white in colour, and for the most part readily separated from the surrounding tongue muscles by blunt finger dissection. During this dissection, the anæsthetist pushed downward on the dorsum of the tongue, thus greatly facilitating removal of the cyst. A Penrose drain was left in the depths of the tongue muscles, the divided mylohyoid muscle sutured with interrupted stitches and the wound closed in the usual manner.

The drain was removed in 24 hours, at which time the patient felt quite well, being able to eat a soft diet. The stitches were removed on the fourth postoperative

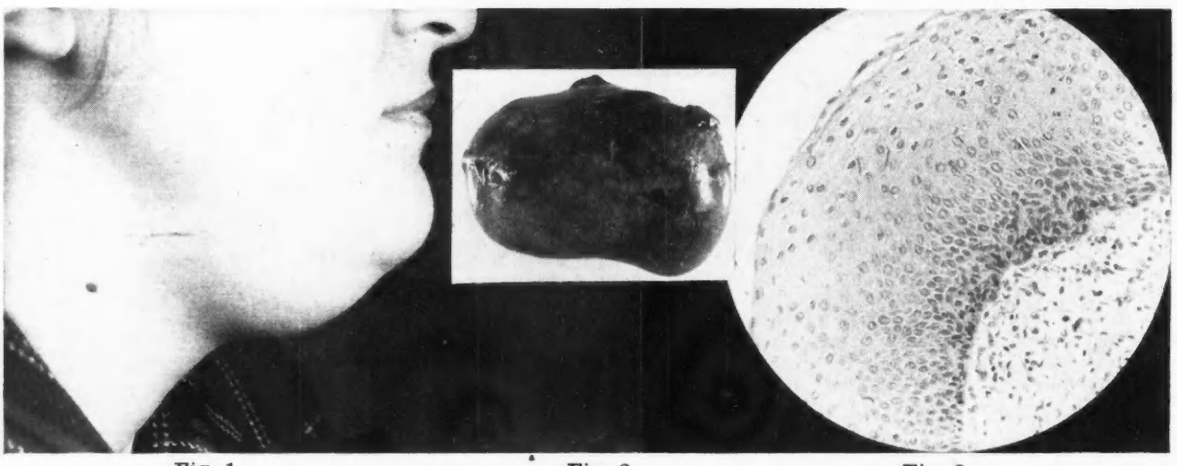

Fig. 1 **Fig. 2** **Fig. 3**

Figs. 1, 2 and 3.—The submental swelling; the cyst; the lining of the cyst.

day and due to the location of the incision the scar was barely noticeable.

The cyst measured 7 x 5 x 5 cm. (Fig. 2) and when opened was found to contain a greasy, grumous material with innumerable minute yellow granules. On microscopic examination the cyst was found to be lined with a simple stratified squamous epithelium, there being no evidence of hair follicles or sebaceous glands (Fig. 3).

COMMENT

Congenital inclusion dermoid cysts develop along the lines of embryonic fusion. Dermoid cysts in the sublingual and submental regions are derived from the ectoderm sequestrated during the union of the first and second branchial arches. These cysts may be either above or below the oral diaphragm (mylohyoid muscle) and therefore may present mainly in the sublingual or submental positions. Rarely, the cysts become dumbbell-shaped by pushing through the fibres of the mylohyoid muscle, thus presenting both above and below this muscle. These cysts are usually in the mid-line but during the growth of the cysts, they may be displaced to one or the other side of the mid-line. The cysts are almost invariably lined with a simple squamous epithelium.[1]

The patients usually present themselves in the 'teens or early twenties, complaining of a double-chin, a swelling in the mouth, difficulty in articulation and occasionally difficulty in mastication. These cysts must be differentiated from ranulas, cystic hygromas, thyroglossal duct cysts, branchial cysts, lipomas, neurofibromas, ectopic thyroids, chronic suppurations, tumours of the submaxillary glands and cold abscesses.

The main complication of these cysts is infection, which may be blood-born or due to a mistaken diagnosis and an attempt at drainage. The infection may spread rapidly and cause acute laryngeal obstruction. Once these cysts have been infected they are very difficult to remove. In such circumstances, New[2] advises cauterization of the epithelial lining.

The smaller sublingual dermoids may be removed through a median sublingual incision. However, if they are large enough to present in the submental region, an incision should be made in this region.

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RUPTURED INTERSTITIAL PREGNANCY*

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The following case of ruptured interstitial pregnancy is reported, together with a brief review of the literature relative to this condition.

The patient, aged 36, para 7 and gravida 9 was brought to the Outdoor Department by ambulance July 13, 1949, in a state of collapse. She stated that her last menstrual period was March 20 and approximately three weeks later she began to experience intermittent sharp pain in the right lower quadrant but this did not prevent her from continuing her household duties. On April 16 she had a small amount of vaginal bleeding lasting only a few minutes. About this date she began to have morning nausea, swelling and tingling of her breasts, and she considered that she was pregnant. On May 14 "spotting" recurred and she reported to her family doctor who confirmed the pregnancy and advised her that she was threatening to abort. Within two weeks her right lower quadrant pain became more constant and more severe and her abdomen which was hard and tender also appeared swollen. She went to bed for three or four days in June and when she felt somewhat better got up and resumed her duties. Although she felt ill, she continued to be up and about for another two weeks. On July 11 during intercourse she experienced an excruciating pain in the lower abdomen and with this she felt "frozen" to the bed. This pain persisted for two days. On the second day it was associated with nausea and vomiting and she was brought to hospital.

On admission the patient was obviously in a state of shock. She exhibited marked pallor, sighing respirations, complained of intense thirst and at frequent intervals cried out with pain. She was fully conscious but was obviously *in extremis*. The pulse was extremely rapid and thready and the blood pressure was not obtainable. Examination of the heart and lungs was not contributory. The abdomen was immobile and the lower portion appeared markedly distended. On palpation it was board-like and extremely tender throughout. An ill-defined mass was outlined in the lower abdomen but the patient resisted any further attempts at palpation and she also resisted pelvic examination. Rectal examination elicited extreme tenderness on touching the cervix and had to be discontinued.

A diagnosis of ruptured ectopic pregnancy with massive intra-peritoneal hæmorrhage was made. Five hundred c.c. of blood and a like amount of plasma were started and the patient transferred to the operating room. Under anæsthesia a pelvic examination was performed and an enlarged uterus about the size of a 3 to 4 months' pregnancy was felt. It was asymmetrical on the right side, the asymmetry being caused by a circumscribed bulging of the right cornu. The adnexæ were not palpable and because of this a diagnosis of ruptured interstitial pregnancy was made.

On opening the abdomen the peritoneal cavity proved to be filled with fluid blood and clots. The uterus was about the size of a 3 months' pregnancy and markedly asymmetrical, the right tube and round ligament arising about 2½ inches higher than the left. There was a large jagged rent on the anterior surface of the uterus with amniotic membranes bulging out and the torn umbilical cord extending from the sac. The fetus 6" long was found lying near the splenic flexure of the colon. On lifting the uterus another rent was found in the posterior surface of the fundus at the placental site. This was bleeding profusely.

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A subtotal hysterectomy and right salpingo-oöphorectomy were performed, most of the blood clot was removed and the abdomen closed without drainage. At the close of the operation the blood pressure was stabilized, the radial pulse was palpable and the patient warm and her general condition much improved. She made a good recovery and was discharged on the 13th day.

Pathological report.—Specimen consists of a 17.0 cm. (crown to heel) fetus, the umbilical cord of which is attached through a rent in the fundus of a fetus that has been amputated at the cervix and the right Fallopian tube and ovary. Uterus measures 13.0 cm. in length and 9.0 cm. across the fundus. There is a tear in the fundus through which protrudes clot, shaggy placental tissue and amniotic membranes. The uterus is distorted by the thickened and widened fundus and tilted toward the right. Transverse longitudinal section through the uterus reveals a large cavity 7.0 cm. in length filled with spongy endometrium. Separated from the upper end of the canal in the right horn is a cavity in the myometrium now measuring 6.0 x 4 cm. exposing fixed placental tissue and an opened amniotic sac. On further exploration the placenta is seen to be attached in the line of the isthmus of the Fallopian tube. A probe passed down the tube passes directly into the placenta and probe passed up from the uterine cavity also leads into the above described space so that the interpretation is an interstitial tubal pregnancy.

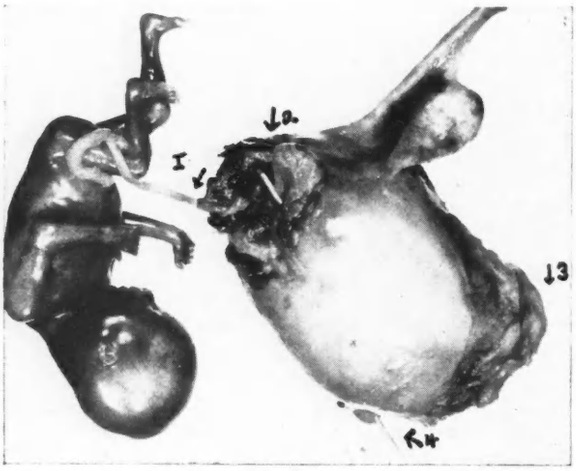

Fig. 1.—Specimen shows rent in fundus of uterus with protruding placenta and amniotic membranes. Arrow (1) points to site of rupture of umbilical cord. Probes inserted in cavity in right horn of uterus (2), the cervix (3), and the stump of right adnexa (4).

Ectopic pregnancy in the interstitial portion of the tube while not a rarity is relatively uncommon. Wynne[1] reviewed much of the literature and up to 1914 had collected 85 cases and added two cases of his own. Again in 1929[2] he reported two cases and at that time had found 163 cases in the literature. Thunig[3] in 1944 reported two cases and found that 199 cases had been reported.

The proportion of ectopic to intra-uterine gestation is about 1:200 although some reports would indicate a greater frequence. Jarcho[4] in his own series gives an incidence of one ectopic in every 69 pregnancies and in every 44 gynæcological admissions. From this clinic an incidence of one ectopic in every 79 gynæcological admissions was reported,[5] 6.3% of the cases being of the interstitial type. The collected statistics from nine authors[4] showed that 4.24% of all ectopics occur in the interstitial portion of the tube. Interstitial pregnancy is thus of particular interest and importance. It differs from the more common forms of ectopic pregnancy in that the greater vascularity of that part of the tube makes it a most hazardous site.

Diagnosis prior to operation is not easily made. Before rupture it may be confused with an intra-uterine pregnancy, a threatened abortion with fibromyoma or pregnancy in a septate or bicornuate uterus. Actually the signs and symptoms are those of any ectopic pregnancy, *viz.*, amenorrhœa, pain and vaginal bleeding plus the palpation of a mass in or about the uterine cornu. After rupture the extreme abdominal and pelvic tenderness renders examination difficult. Rupture usually occurs between the second and third months and is very rare after six months.[4] It may follow coitus or exertion. The usual site of perforation is the posterior surface of the uterus into the peritoneal cavity although it may rupture into the broad ligament.

Prompt surgical interference should always follow a diagnosis of ectopic pregnancy and in a case of the interstitial type immediate operation by the abdominal route is imperative. Supravaginal hysterectomy is usually the operation of choice. The usual methods of combating shock and internal hæmorrhage are employed and any delay in instituting restorative measures invites disaster. Operation should be withheld while the patient is in a state of secondary shock but during the time that the operating room is being prepared the patient will usually respond to transfusion of whole blood and plasma. A successful outcome depends most upon maintaining the blood volume. Whole blood must be given and in adequate quantities to restore the blood pressure and pulse. This must be kept up postoperatively until the patient's condition is considered satisfactory.

SUMMARY

An unusual case of ruptured interstitial pregnancy has been presented. Rupture occurred during the seventeenth week of gestation. We wish to emphasize the necessity for an awareness of this type of ectopic pregnancy when the history of ectopic may be typical with no adnexal masses palpable to substantiate it. In

a case where rupture has not occurred and the diagnosis is in doubt a gentle pelvic examination under anæsthesia may help to elucidate the true condition.

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INTERSTITIAL PREGNANCY*

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[*The general features of interstitial pregnancy have been discussed in the preceding paper. The following report, which was received a few days later, is another instance of this rare condition.*—EDITOR.]

M.G., a 33-year old single girl, was first admitted on June 19 with vaginal bleeding.

Her story was that about the middle of May she had attempted a self abortion with a knitting needle. This caused pain and some vaginal bleeding but did not initiate any labour pains. She continued about her usual work and although her breasts "softened" she felt that her attempt had been unsuccessful. This brownish discharge continued until about three days prior to entry. She then took quinine in large quantities, and was violently sick. The day before entry she had some increase in the bleeding.

On the day of admission she developed suddenly a severe pain in right lower quadrant about four p.m., with a feeling of faintness and a gradually developing ache on top of the shoulders.

On admission she looked very ill. However, the temperature was 98.6°, Hb. 90%, red blood cells 4,050,000, white blood cells 9,000, blood pressure 96/65. She seemed in severe pain and pulse was 130. Because of the tenderness pelvic examination was difficult but it was felt that the uterus was about 4 months' pregnant, with cervix softened but closed. Pelvic findings suggested a peritonitis and it was thought to be the result of interference. She was given intravenous fluids, penicillin and 500 c.c. of blood as a therapeutic measure. We were surprised the next day, however, that the temperature was only 99°. Pulse was 88, white blood cells only 10,400 and abdomen still showed signs of peritonitis. She still had some vomiting but felt considerably better.

On the 22nd her penicillin was stopped and she was allowed up, and the following day she felt well enough to be discharged. Recheck showed the uterus "size of 3 months, hard, and probably still containing a pregnancy".

Next day about ten a.m. her original pain returned with greater severity in lower abdomen, fairly generalized, steady but with crampy exacerbations "like labour pains". The shoulder pain was again felt. This attack was much more severe and she was again rushed to hospital.

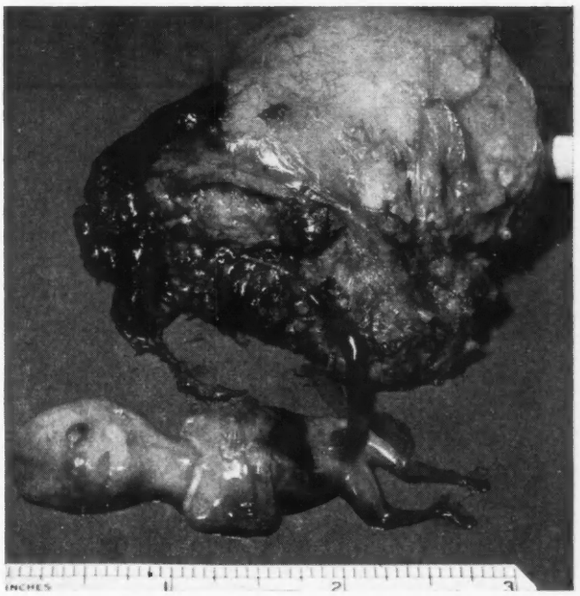

Fig. 1.—Showing situation of rupture. A pencil is inserted in the cervix.

She looked very ill again but was much paler, somewhat shocked and irrational. Signs of peritonitis with free fluid in the flanks were quite definite. Cervix was slightly soft, bluish and very tender to move, uterus not outlined because of tenderness and guarding and there was slight bleeding from cervix with a doughy feeling in the right fornix. Hgb. 62%, white blood cells 17,400, red blood cells 3,050,000, blood pressure 90/0, temperature 96. A diagnosis of intra-abdominal hæmorrhage was made, from ruptured ectopic pregnancy on the right side, and she was taken to the operating room.

The peritoneal cavity was full of dark blood which was regarded as probably too old to be used for auto-transfusion. Some of this was mopped out and exploration of the pelvis

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ruptured the sac which was situated on the right corner of the uterus in the intestitial portion of the tube. Remainder of tubes and ovaries both normal. A fetus about 10 to 12 weeks was found in the vicinity. The upper right corner of the uterus was grossly disorganized from the rupture which had occurred so a subtotal hysterectomy was quickly done. With the aid of four transfusions and oxygen, immediate recovery was good, and patient was discharged on the 9th postoperative day in good condition.

PSEUDOHERMAPHRODITISM*

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In contrast to true hermaphroditism in which both male and female gonads are present in the same individual, and of which there have been only some twenty proved cases collected from the literature[1] pseudohermaphroditism is a relatively common condition. Statistics indicate that it occurs once in 1,000 persons.

Pseudohermaphroditism exists when the gonads are of one sex only, but some or all of the secondary sex characteristics are of the opposite sex. A pseudohermaphrodite is classified as male or female depending on whether the gonads are testes or ovary respectively; and as external, internal, or complete depending on whether the external, the internal, or all the secondary sex characteristics conform to those of the opposite sex from the primary gonad. Most external and complete pseudohermaphrodites are brought up as the wrong sex, and if they marry, marry a member of the same sex.

Pseudohermaphroditism is much more common in females than in males. In the great majority of cases it is of the congenital variety, stigmata being present from birth, and the ovaries possessing a fairly normal histological structure. In others it is acquired as the result of hormonally active virilizing tumours of the ovary or adrenal cortex. Whether hormonal influences in embryonic life may contribute to the development of the congenital variety is still purely a matter of theoretical consideration, and hormone assays have not so far thrown any light on the matter or enabled a differentiation of pseudohermaphrodites into male or female. The diagnosis depends on laparotomy and often on microscopic examination as well.

The following case report is presented as a rather rare example of pseudohermaphroditism.

Miss D., aged 40, was admitted to the hospital for investigation of absence of menstruation. Of normal feminine external appearance, slender build and quite attractive, she had never menstruated; consequently she had never considered marrying, though feminine in her emotional make up.

Family history revealed that the patient had an aunt of normal feminine appearance, who died at the age of 70 without ever having menstruated. There was no other unusual feature in the family history. The patient has four sisters all of whom menstruate normally and are married, three of them having children. There are two brothers who are normal.

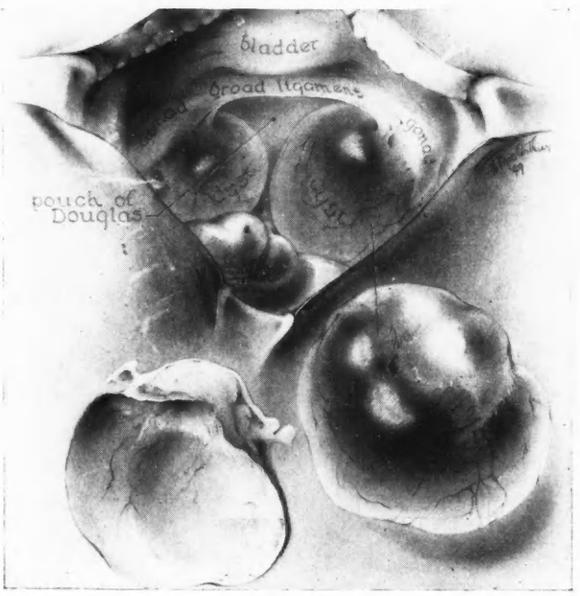

Fig. 1

Personal history revealed that shortly after birth the patient was found to have bilateral inguinal masses, which were considered to be herniæ, and were replaced in the abdomen, the patient wearing a truss until the age of fifteen. Apart from failure to menstruate nothing abnormal was noted. Breast development, and general external appearance were quite typically feminine, as were the voice, manners and libido.

On physical examination: skin was soft and dry; pelvic and axillary hair was scanty, there was no facial hair; breasts were moderately well developed except for the nipples which were small; chest and cardiovascular system were normal; there was fullness of the lower abdomen with no tenderness.

Pelvic examination: vulva was normal; vagina had a normal introitus, but ended blindly about 1 inch beyond the hymeneal orifice which admitted the tip of a finger; there was no sign of cervix, but recto-abdominal palpation revealed the presence of bilateral pelvic masses.

Cystoscopic examination was performed and catheters passed up the ureters. The bladder seemed to be grossly enlarged and atonic. Urinalysis and hæmogram were normal.

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Laparotomy was carried out. The pelvis was filled by two cysts arising from gonad-like tissue on either side of the broad ligaments (as shown in Fig. 1) which fused in the midline. There was no sign of uterus or tubes. The gonad-like structures ended blindly in firm fibrous strands which fused into the "broad" ligaments; they were clamped low down and removed along with the cysts.

Microscopic examination: the cyst removed from the right side measured 14 x 10 x 8 cm.; it was thin-walled and smooth and contained clear fluid. It consisted of one large locule and a few small locules. The cyst from the left side was similar only smaller, measuring 4.5 x 3 x 2.5 cm. The cysts arose from solid tissue which grossly resembled gonads. On each side this measured approximately 3 x 2 x 2 cm. and section revealed firm greyish yellow tissue having a smooth greyish blue capsule 0.2 cm. thick. These two structures ended in firm fibrous strands.

Microscopic examination of several sections through the structures which grossly appeared like gonads revealed gland-like tissue separated off into lobules which were made up of a profusion of tubular structures having the characteristics of testicular tissue with a considerable amount of interstitial cells. The tubular elements were of the immature variety; only very few showed a lumen and there was no evidence of spermatogenesis. The structure was orderly; the cells appeared benign; the interstitial cells varied considerably in size; there were some cytoplasmic inclusions seen, but no rod-like mitochondria. Section through the fibrous strands showed a mixture of smooth muscle and connective tissue fibres without any characteristic arrangement; there was no evidence of a lumen or of glandular components. Sections of the cyst wall showed a dense fibrous capsule; the lining was of low columnar epithelium; no goblet cells or cilia were seen. The two sides were similar, and of many sections taken there was no evidence of ovarian tissue, nor any definite evidence of either the Müllerian or Wolffian tract derivatives.

The diagnosis was made of male gonads, immature, undescended, with cyst formation. No sign of other gonads were found either in the peritoneal cavity or the inguinal canals.

This therefore appears to be a case of male pseudohermaphroditism with feminine external and complete absence of internal accessory sex characteristics. Very similar cases have been reported by Novak[2] and by Greenhill and Sahunitz.[3] Unfortunately no hormone assays were performed in this case which however fairly obviously represents a congenital type of pseudohermaphroditism.

Removal of the gonads at this time, as would be expected, had no influence on the patient's external appearance. A year later she is in good health; and there has been no change in weight; and no symptoms of a menopausal nature such as "hot flushes", though the patient did go through a period of emotional upheaval. This was only temporary and she has made a good adjustment to the acceptance that her sexual organs were abnormal, though the true nature of her sex was not explained to her.

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LIPOMA OF THE CHOROID PLEXUS

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Approximately 80 cases of lipomas of the central nervous system have been reported, most of them having originated in the corpus callosum. In the majority of these cases, according to Scherer,[1] the corpus callosum was either poorly developed or even completely lacking. The base of the brain is also a common site for these growths. Few have been reported in the choroid plexus; of these 10 were solitary lipomas and 6 accompanied other lipomas of the central nervous system. In general, lipomas found in the choroid plexus have been quite small and innocuous, and most of them were accidental findings at necropsy.

In view of the rarity of this location it is deemed worthwhile to report a case of solitary lipoma of the choroid plexus and to present a brief review of the literature.

A 36-year old woman was admitted to the Saskatchewan Hospital at Weyburn, Sask., with acute mania. On the fourth day after admission she developed a bilateral parotitis and died one day later. On gross examination the brain showed no alterations, except for a small oval nodule about 0.5 mm. in length, which was found in the choroid plexus of the central part of the left lateral ventricle, in the region of the glomus choroideum.

Microscopically, the nodule consisted of typical mature, adipose tissue. The fat cells were large, regular in outline, and had eccentric nuclei. Psammoma bodies were scattered throughout the tumour between the fat cells (Fig. 1). The whole structure was separated from

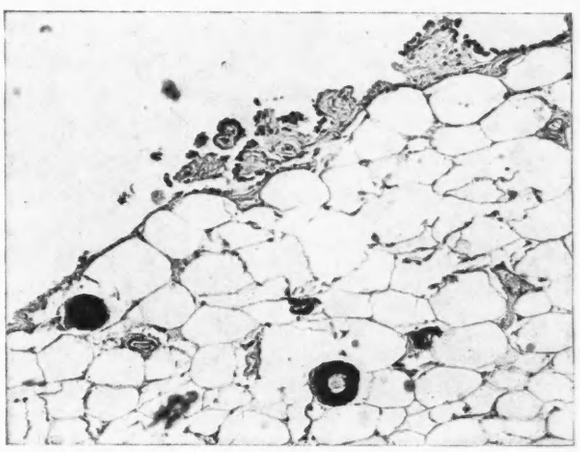

Fig. 1

the surrounding tissue by a thin, connective tissue capsule with some plexus tufts, and the latter was covered by a single layer of normal choroid plexus epithelium. Beyond doubt this structure has to be considered a lipoma. The choroid plexus in the vicinity was normal and contained scattered psammoma bodies. The microscopic examination of the brain proper revealed no pathological changes.

COMMENT

Lipomas situated in the choroid plexus are rarely accompanied by definite clinical manifestations; in this respect they resemble other intracranial lipomas. It is most likely that this failure to manifest symptoms is responsible for the fact that only a few cases have been reported. Their main interest is evoked by their apparent rarity and by their origin.

In 1935 Krainer[2] reviewed the literature. He listed 8 lipomas that had been described in the choroid plexus. In addition he notes 3 cases in which lipomas of the choroid plexus were combined with similar lipomas in the corpus callosum. He also mentioned Obersteiner's case of a lipoma in the medial choroid plexus of a duck. In a thorough review of the literature (1945), Ehni and Adson[3] mentioned one case described by Simon and cited by Scherer in 1935. This case could not be traced and should be accepted with reserve. Liber and Lisa[4] recorded one lipoma of the choroid plexus in 1940.

A number of theories have been advanced to explain the occurrence of fat tissue in the brain. In one of these theories it is maintained that lipomas arise by the metaplasia of embryonic tissue remnants left over when the nervous system was formed. Krainer on the other hand considered them to be formed by the "heterotopic differentiation of cells of the persistent primitive meninx". In another theory it is suggested that they are formed by the late metaplasia of mature connective tissue of the pia. Still other investigators believe that lipomas of the central nervous system arise from the same mesenchyma from which the blood vessels of the choroid plexus are formed.

SUMMARY

Lipomas of the central nervous system are relatively rare, those of the choroid plexus extremely so, although it is very probable that many such cases are not being reported in the literature. A lipoma of the choroid plexus found at necropsy is described. It seems to be the eleventh case of a solitary lipoma of the choroid plexus hitherto recorded.

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DIPLOCOCCUS MUCOSUS (LINGELSHEIM) SEPTICÆMIA IN AN INFANT*

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In 1906, during an epidemic of meningococcal meningitis in Upper Silesia, Germany, while he was examining throat cultures to find meningococci, v. Lingelsheim,[1, 2] discovered a diplococcus which morphologically resembled the meningococcus, but differed from it in cultural characteristics. It grew on ordinary media in the first culture and produced mucus. Therefore, he named it *Diplococcus mucosus.*† He also found it once in a culture of spinal fluid of a patient who had pneumonia.

In later years there have been a few publications,[3 to 7] in which this organism was reported to have been cultured from spinal fluids of patients suffering from meningitis. We were unable to find any report of the *Dip. mucosus* having been grown in blood culture.

In cases of meningococcæmia petechial hæmorrhages in the skin are observed quite commonly as part of the clinical picture. They may be encountered less frequently when other microorganisms invade the blood stream. Such an instance due to *Dip. mucosus* septicæmia in an infant forms the basis of this report. It is of interest not only because of its rarity but also because it illustrates the importance of blood culture for exact diagnosis in similar conditions.

J.L., a 6-month old female infant, was admitted to the Pædiatric Service, Jewish General Hospital, October 6, 1948. The chief complaints were fever, skin rash, malaise, and anorexia. She was well prior to October 3, 1948, when she developed fever. She refused much of the food offered her and lost her usual cheerfulness. The fever rose to a high degree several times since the onset. A rash on the legs and trunk was first observed by the mother on October 3. It became more pronounced during the 3 days before admission. No vomiting was noted. There was an occasional loose stool but no real diarrhœa. On the day of admission, the legs were somewhat swollen and the baby cried when they were moved.

She was the only child of young healthy parents. There was no known exposure to any sick person. Her feeding was adequate and she had gained weight regularly since birth. She had been given some cod liver oil but no orange juice or ascorbic acid. She had not been vaccinated or inoculated against any disease.

Physical examination revealed a large, well nourished baby who appeared acutely ill. The weight was 19 lb. 6 oz. The temperature was 105° F. The cheeks were flushed. Petechiæ were present over the lower extremities

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† According to Bergey's Manual VI. ed. p. 301 the diplococcus is classified as a member of the family Neisseriæ, but carried under the name *Diplococcus mucosus von Lingelsheim.*

and to a lesser extent over the trunk and upper extremities. There was swelling as well as increased heat surrounding the left ankle, which showed slight pitting on pressure and was painful on movement. Some fullness seemed to be present about the right knee. The tip of the spleen was palpable. There was no rigidity of the neck. The anterior fontanelle was level. The ocular fundi were normal. No teeth had erupted and the gums appeared normal. Leukocyte count was 16,000 per c.mm. An intradermal tuberculin test (1:1,000) and a blood Kline test were negative. Urinalysis was negative.

It was felt that the infant had a septicæmia, possibly meningococcal, with involvement of the left ankle and right knee.

Laboratory findings.—The spinal fluid was clear; the pressure was 350 mm. initially and 250 mm. after 8 c.cm. were withdrawn. Pandy reaction was negative. A cell count showed 10 leukocytes per c.mm. The sugar content was 85.6 mgm. %; protein, 21.38 mgm. %.

X-ray examination of the chest and long bones was negative except for a slight swelling of soft tissue about the right knee and considerable swelling about the left ankle.

Bacteriological findings.—Smears from spinal fluid did not show any cells or bacteria; cultures remained sterile. A blood culture showed bacterial growth in broth as well as in agar after three days incubation. The organisms recovered were Gram-negative cocci, which in size and shape resembled and therefore were regarded at first as probable meningococci. However, subcultures showed a luxuriant growth on the surface of ordinary agar as well as on blood agar and chocolate agar. No change in the colour of these media was observed. The outstanding feature was the formation of mucus. The organism was therefore identified as *Dipl. mucosus* (Lingelsheim).

Tests for sensitivity of this organism showed it was not affected by 1 unit of penicillin, but it was sensitive to 0.1 gm. streptomycin.

The organisms were agglutinated by the patient's serum (taken the day before discharge) up to a dilution of 1:16, whereas 5 control sera gave negative results.

Throat cultures from the patient and her parents failed to show the diplococcus. Unfortunately no culture was made from the petechial skin lesions.

Treatment and course.—The infant was given 0.39 gm. of sulfadiazine orally every 4 hours, and 30,000 units of penicillin intramuscularly every 3 hours until October 17. Thereafter, because there was still some swelling of the right ankle, although movements were free and apparently painless, and because the organisms were penicillin resistant, 30,000 units of streptomycin were administered intramuscularly every 3 hours for 7 days.

The temperature dropped rapidly and was normal 48 hours after the infant's admission to the hospital. By this time she no longer looked very sick. Roentgenograms of the lower extremities just prior to leaving the hospital showed no abnormalities. The patient was sent home on October 28, completely recovered.

HÆMATOLOGICAL FINDINGS

Date	*R.B.C. million*	*Hgb. %*	*W.B.C.*	*Poly.*	*Ly.*	*Mon.*	*Eos.*	*Stab*	*Ret.*	*Rumpel-Leede*
October 8	2.79	52	18,800	64	22	9	1	9		pos.
" 15	3.14	63	9,000	58	26	10	1	5	1%	neg.
" 20	3.00	61	7,300	48	42	6		4		
" 26	3.52	70	6,000	24	55	12	8	1		

Bleeding time and prothrombin time were normal. There was a slight normochromic dimorphic anæmia.

DISCUSSION

In many instances of infection of the meninges as well as of the blood stream associated with petechial skin lesions, when no micro-organisms are grown in cultures of spinal fluid or blood, it is assumed that the meningococcus is the culprit. This may often be correct. That one cannot be certain that this is so in the absence of corroborative bacteriological evidence is well illustrated in this instance.

Whereas most of the reported cases of *Dip. mucosus* infection occurred in malnourished children or following operations for cerebral tumours, this infant was well until the onset of the infection.

All of the patients died prior to the advent of sulfonamides. Only one case[4] is reported to have recovered following treatment with sulfapyridine. The rapid improvement following the administration of sulfadiazine in the present instance and the recovery obtained in the case of Bray and Cruickshank[4] would make it appear likely that sulfonamide therapy had a good effect. Streptomycin, to which the organisms were found to be sensitive *in vitro*, was begun only after the infant was already on the road to recovery. It was given because the left ankle was still considerably swollen. It may have contributed in some measure to the final complete recovery; it is possible of course that this might have occurred without it.

Of other Gram-negative diplococci the *Dip. mucosus* seems to resemble most closely the *M.* catarrhalis. They have in common: morphology, staining characteristics, nutritional requirements, sugar fermentation reactions (Table I). In the human body both may be found in the nasopharynx as saprophytes. Only rarely do they produce infection by invading the blood-stream and/or the meninges. The formation of mucus by the *Dip. mucosus* differentiates it from *M. catarrhalis.*

TABLE I.

Sugar	*Fermented by*			
	Meningo-coccus	*Gono-coccus*	*Micro. catarrh.*	*Diploc. mucos.*
Glucose	+	+	−	−
Saccharose	−	−	−	−
Maltose	+	−	−	−

SUMMARY

A case of septicæmia in an infant 6 months old with a clinical picture resembling meningococcæmia is reported. Petechial lesions were present. There was also swelling of the left ankle and to a lesser degree of the right knee. Blood culture yielded a pure growth of *Dip. mucosus* (Lingelsheim). No record of any such previously reported instance was found.

Treatment with sulfadiazine and streptomycin was followed by complete recovery. It is doubtful if penicillin, which was given, was of any value, since the organism was found to be penicillin resistant to 1 unit.

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POLIOMYELITIS: A CASE POSSIBLY DUE TO INTRACUTANEOUS INOCULATION*

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So far as we have been able to determine, two cases only have been reported of poliomyelitis in laboratory workers who were exposed to the virus in the course of their work. In one of these, a 26-year old male, the possibility of intracutaneous inoculation was entertained.[1] In the other, a 35-year old female, there was no evidence that the route of infection was by the way of inoculation.[2]

The evidence for or against any particular route in either of these cases is far from conclusive. The duties of both workers consisted of the grinding of tissues from cases of poliomyelitis in preparation for inoculation into monkeys. In one case[1] a possible portal of entry was provided when a non-infected monkey scratched the worker on the wrist. Following a period of 12 days after the scratch a widespread paralysis appeared and was progressive until death. Poliomyelitis virus was isolated from the axillary lymph nodes of that arm. The authors suggested that the point of entry was the abrasion. The other case was less conclusive and concerned a non-fatal but paralytic illness which developed 12 days after the patient left the laboratory on a holiday.

In addition, Leake[3] has reported a series of 12 cases of paralytic poliomyelitis amongst many thousands who received trial vaccination against the disease. The incidence amongst those inoculated was sufficiently greater than amongst those not inoculated to warrant consideration of the possibility of intracutaneous inoculation as the source of infection. Further, it was postulated by Sabin and Ward[4] that a cutaneous disruption was the site of entry in the case of a 29-year old male physician who was doing research on poliomyelitis. He was bitten on the finger by an apparently normal monkey, 13 days before the typical picture of an ascending myelitis developed, from which he died four days later. The pathological findings suggested a virus etiology as the basis of the lesions in the central nervous system, and a virus subsequently termed "B" virus, similar in many ways to the virus of herpes, was isolated from the brain and spinal cord. A clinically and pathologically similar disease was then produced in two series of rabbits by the inoculation of the brain and spinal cord of the patient into the first series of rabbits, and in turn by inoculation of the same organs of that group into a second series of animals.

The infrequency of cases such as these prompted this report of the case of a 28-year old pathologist, who contracted poliomyelitis while on the autopsy service of this institute and who was without any known living contacts.

On August 27, 1949, this doctor carried out a post-mortem examination on a 26-year old female who had died 12 hours previously of the bulbar type of poliomyelitis. Following the autopsy, in which the brain and spinal cord were removed, his finger was accidentally punctured by the needle which was being used to close the dorsal mid-line incision. One week later he developed general malaise. In the second week there appeared progressive complaints of severe bilateral frontal headache, which lasted only 12 hours, and lumbar discomfort, which gradually spread into the cervical region. The temperature ranged from 101 to 102°. Lassitude developed and vague ill-defined areas of hyperesthesia were noted scattered over the limbs and trunk. Just prior to admission to hospital, nausea, vomiting, and, finally, urinary retention commenced.

On admission on September 14, 1949, the temperature was 100.2 degrees. The patient was agitated and irritable. All reflexes were hyperactive, and many vague hypersensitive areas of skin were described, as above. Stiffness of the cervical spinal column was moderate and Kernig's sign was moderate bilaterally. The spinal fluid

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pressure was normal, cell count was 250/c.mm., with a predominance of lymphocytes, and the protein content was 150 mgm. %. Three days following admission, moderate weakness of the extensors of the right toes and foot was first noted. A clinical diagnosis of acute anterior poliomyelitis was made at this time. Progress was fairly satisfactory thereafter, and at the date of writing (May, 1950) only minimal weakness of the right anterior tibial and of the right pectoralis groups of muscles persists.

DISCUSSION

Intracutaneous inoculation as a mode of infection in man has been suggested on very few occasions in the field of virus infection in general,[4, 5] and with even less frequency in the field of poliomyelitis.[6, 7] Although it is understandably impossible to state with certainty that any one case is without doubt one of intracutaneous inoculation, this case is presented for consideration. The possible incubation period from the day of suggested infection until the onset of the malaise was seven days, and until the onset of the headache and the lumbar discomfort it was 10 days. There were a few days of regression of symptoms before the return of the lumbar discomfort and the progression of the disease, as above described. Paralytic signs first appeared on the twentieth day after the day on which infection is considered to have occurred. The onset of the illness would correspond closely with the infection occurring about the date on which the autopsy was performed. It is unlikely that the infection could occur from a dead body other than in a percutaneous manner. Since in this case conditions existed for such infection, there appears to be a high degree of probability that infection was by the way of intracutaneous inoculation. For this reason, we feel that sufficiently pertinent facts exist in this case to warrant its publication for its informative value in the literature.

In older texts on poliomyelitis the failure of the disease to spread on hospital wards or to nurses or attendants of cases was looked upon as evidence against the spread of the disease by ordinary mechanisms of contagion. It is now clear that in view of the fact that infection with the virus of poliomyelitis is predominantly subclinical, incidences of obvious contagion would hardly be expected as frequently as in the more common infectious diseases. Even in the experimental animal, successful inoculation varies markedly with different routes; intracerebral inoculation is most effective, intranasal instillation comes next, subcutaneous inoculation is still less effective, and intracutaneous injection of the virus is least effective, of all. In an experiment in which immunization was attempted with active virus, Aycock and Kagan[8] found that only one of twelve animals receiving multiple intracutaneous injections of active virus developed the disease. In view of these considerations, more importance probably should be attached to the relatively small number of laboratory transmissions of the disease which have been reported.

SUMMARY

A case of poliomyelitis has been presented with a view to its inclusion in the small group of cases considered tentatively to have been contracted via the intracutaneous route.

The author wishes to record his grateful appreciation of the interest of Dr. F. L. McNaughton and Dr. G. Lyman Duff in this case report. He is indebted to Dr. W. Lloyd Aycock of Harvard University for valuable criticisms and suggestions.

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SPECIAL ARTICLE

THE LIFE AND OUTLOOK OF THE NATIVE IN SOUTH AFRICA*

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Africans may be divided roughly into two classes—the sophisticated and the unsophisticated.

The more or less sophisticated, town-dwelling Native, who may have a smattering of education, has usually acquired something of the white man's civilization. He knows a little of the importance of personal cleanliness, and he lives under fairly hygienic conditions. Often enough, he apes the diet of the European: but his wages are low; meat, fruit and vegetables are expensive; and, since he knows nothing of food values, he pays no attention to these important items. Unless, therefore, he is properly fed by his employer, he is as prone to nutri-

* Extracts from material kindly supplied by Dr. J. B. Ritchie from his impressions on a recent visit to South Africa.

tional disorders as is his less sophisticated brother. All the same, he is gradually acquiring the habit of seeking medical attention from the white doctor, and is beginning to realize that the latter's medicine is more efficacious than the remedies of his own people. But it is of importance to appreciate that very many of these Natives—even though they may profess the Christian religion—are still ridden by the perhaps subconscious fear that, by consulting a white doctor, they may be provoking the wrath of the spirits of their ancestors. Many, therefore, will prefer to consult their own herbalists or diviners, or even to seek no attention. The town-dwelling Native has usually a smattering of English, and the European doctor is, therefore, better able to examine him than he is able to examine a Native straight from the kraal.

The vast majority of Africans are unsophisticated. They live in their reserves and seldom come into contact with the white man. Their villages are badly planned and are often situated in malarial or tsetse-fly areas. They know nothing of the importance of taking precautions against disease. They have no idea of cleanliness, and their huts are breeding-grounds for parasites and germs of every kind. Of sanitary arrangements they know nothing at all. They wash and bathe in the rivers in which they deposit their excreta, thus continually infecting themselves with bilharziasis. Their methods of agriculture are very poor, primitive, short-sighted and often disastrous, with the result that drought and famine frequently supervene. As a whole, their diet is extremely poor, consisting mainly of maize and other starchy cereals. Avitaminosis is common. Their resistance to infective diseases is weak. I may mention, however, that from earliest childhood all the Bantu races consume kaffir beer. Fox (1938) has reported on the value of this beverage as a source of vitamins C and B.

WITCHCRAFT AND MEDICINE

As every doctor knows, the patient's outlook is always of interest and sometimes of importance. The medical man, practising amongst Natives, will at once perceive the curious indifference of the sick African. Compared with the European, he displays—or appears to display—little or no interest in the outcome of the illness which has attacked him. This is because almost every sick African attributes his illness to supernatural causes and because he fears that, by consulting a white doctor, he is provoking—or further provoking—the spirits of his ancestors. These beliefs are inherent and are, I venture to say, at the backs of the minds of even those Natives who have embraced the Christian religion.

The direct results of this unfortunate outlook are a lack of confidence in his treatment and a fear that, even if he is cured, some worse thing may befall. Such a state of mind is, indeed, next door to fatalism, and if once an African makes up his mind that the spirits of his ancestors are irrevocably opposed to him, he feels that it is useless to fight against their decision. It follows that though a prognosis may be fair, once a Native decides that he is doomed, the chances of his recovery are greatly impaired; and, though he may not have come to such a conclusion, he has never the same incentive as the European to fight a dangerous illness. To obtain such a patient's confidence is practically impossible, and this lack of co-operation with the white doctor is one of the great difficulties of Native practice.

The European is not a fatalist; the African is. The European does not believe in witchcraft or in the power of the dead to affect his well-being; the African does. The only enemies the European knows are those he can see; not so the African. A Christian who falls sick does not consider it incompatible with his religion to consult a doctor; religion and disease are separate entities. But, as I have said before, even the Native who has embraced the Christian faith does not in his heart subscribe to the above tenets.

There are three enemies to the sick African's peace of mind. They are: (1) The spirits of his ancestors or other spirits whom he may have offended. (2) The witch-doctor (nganga). (3) The wizard or witch.

It is to the active ill-will of one or other of these three that the patient, though he will never admit it, *in his heart* attributes the hard fact that he is sick.

The vast majority of Africans, living in the reserves and untouched by our civilization, accept implicitly all the articles of their natural faith; but even the more sophisticated minority who mingle with the European still cling to their original belief in the power of the dead. In other words, nothing will make them believe that they are not to a great extent at the mercy of the spirits of their ancestors, and of certain evil spirits—of enemy tribes or even of animals—which are ever ready to enter and possess the unwary.

The ancestral spirits are, naturally, the most important, and are more venerated and feared than were the ancestors themselves, the dead being credited with supernatural powers. Nothing must be done to provoke them, lest misfortune overtake the offender or his family.

The wizard, or witch, of course, belongs to the realms of superstition, and not to that of piety. Demands upon credulity are, therefore, much heavier. Still, such creatures are credited with certain magical powers. They are supposed to be able to become invisible, to assume the shapes of animals, and to visit their enemies with sickness or death by the spell of the evil eye.

The witch-doctor, or nganga, is, from some points of view, the most dangerous enemy of the three. He is the recognized medium or intermediary between the living and the dead. It is he who keeps alive the dread of an imaginary evil, and it is his art which turns this evil into a reality.

Not all such men are charlatans. Some actually persuade themselves that they are not self-appointed, but have been chosen by the spirit-world. Their supposed selection may have been revealed to them in a dream, or they may believe that they have inherited the appointment, as well as the materia medica, from a father or uncle.

But, charlatans or no, such men are held to be wise and learned doctors, seers or magicians, skilled not only to identify the spirits they serve and to read their will, but even, in some cases, to control them. Some witch-doctors specialize and become pretended authorities upon leprosy, children's disease, fortune-telling, rain-making or lightning-conducting. All are professed masters of the art of bone-throwing—an operation which is supposed to indicate which spirits have been provoked, why they have been provoked, and what penance must be done to propitiate them.

Finally, witch-doctors have to live.

In all these circumstances it is clear that, charlatan or no, the witch-doctor will view the visit of a Native to a white doctor with anything but approval, and that the unhappy visitor is well aware that he is certainly offending the living and very possibly aggravating his provocation of the dead.

From what I have said, it will be clear that the greatest obstacle to such an outlook is the influence of the witch-doctor. This will and must eventually be destroyed; but its destruction presents a problem which, as I see it, can only solve itself after many years. The power of the witch-doctor will decay, just as, centuries ago in Europe, the power of the oracles decayed. But until that time the sick African will endure much unnecessary suffering.

The only way to eradicate witchcraft is by education. Conversion to the Christian faith has done much to shake the coming generation's belief in witchcraft. The teaching and practice of elementary hygiene in the schools has helped considerably in training young Natives to live a more healthy life. An increase in the teaching of physiology would be of further benefit. Too few natives, however, come under the influence of the missionaries and the schools, and many of those who do by no means lose the subconscious fear of evil spirits. The vast majority, of course, are still untouched by this civilization. Many hundreds of schools are needed in the more inaccessible parts of the African territories.

DISEASES COMMON IN THE EUROPEAN, BUT LESS COMMON, RARE OR ABSENT IN THE NATIVE

This group is a large one. Examples here are stomach and duodenal ulcers, cholecystitis and gall stones, which are rare in the Native, but of frequent occurrence in the white man. Acute inflammation of the appendix, one of the most usual causes of the acute abdomen in the European, is seen at times in the Native, especially in areas endemic to bilharziasis. In the primitive Native the disease is apparently distinctly rare, but in the urbanized Native, whose diet may conform to that of the European, it is more commonly encountered. Salpingitis, however, is common in both races.

Other conditions rare in the Native, though often encountered in the white man, are carcinoma of the stomach, pancreas, bowel and rectum. Adenoma or cancer of the prostate is frequently seen in the elderly European, but is distinctly uncommon in the African. Glioma is also of interest, as it is one of the commoner malignant tumours of the European, but rarely encountered in the Native. Carcinoma of the cervix, uteri and the breast are occasionally seen in the Native, but its incidence is less than in the European. However, in my inquiries, carcinoma in the male breast is a more frequent finding in the African. Carcinoma of the kidney and of the œsophagus are not rare conditions in the Native. Melanotic sarcoma accounts for many deaths in the Native, and is far commoner as compared with the European. The tumour may arise in the skin or, as so frequently happens, in the uveal tract of the eye.

With regard to the disorders of the blood, pernicious anæmia (one should here include subacute combined degeneration of the cord), sprue and cœliac disease, well-recognized illnesses in the European, are said to be absent in the African. Leukæmia is seen in both races, but the acute variety appears to affect the Native much more often than the chronic variety. Hodgkin's disease is a fairly frequent condition in the European, but it is certainly less common in the Native.

In considering the cardio-vascular system, coronary disease (coronary thrombosis and angina pectoris) is a particularly common malady in the European, but the African rarely seems to suffer from this. I cannot say the same of high blood pressure, which although especially frequent in the European is not infrequent in the Native. The reason for the lower incidence of these diseases in the Native may be that he is not as exposed to the stress and pressure of life as is the white man. The average duration of life of the African is much less than that of the average European; if he lived longer, hypertensive and coronary disease might possibly be encountered as frequently as in the European. However, it is certainly true,

at the present time, that coronary disease and, to a lesser extent, hypertension are found less often in the African. All doctors have seen an aneurysm of the aorta in the European, at one time or another, but among the Natives of Africa, as a whole, it is very rare.

Rheumatic fever is a common disease, especially in temperate climates. Many believe, wrongly, that it is rarely or never seen in the tropics of Africa. Rheumatic fever affects both whites and blacks in the tropics, but more often the former. Rheumatic fever, however, is not rare in the African. It appears that the typical attacks of the disease encountered in Canada are uncommon in Africa, because the disease tends to run a milder and less striking course in Africa. In the majority of cases the attack seems to consist merely of flitting joint pains with little upset in the temperature. The heart, however, is just as liable to be affected; and mitral stenosis, aortic incompetence and subacute bacterial endocarditis are not infrequently seen in the African. Chorea is not encountered in the Native of tropical Africa, but in the Union it is apparently occasionally seen.

The absence of rheumatoid arthritis in the Native is in marked contrast to its frequency in the European. Gout and hæmophilia, both well-known diseases in the white man, are not seen in the African. However, gout in the European, is rare in Africa. Osteoarthritis, on the other hand, is often encountered in the Native.

The infectious diseases are also of interest, as some of the common ones are seldom or, according to some, never seen in the African. Scarlet fever is very rare in the Native, especially amongst those of Central, South Central, West and East Africa. Diphtheria, although quite common in the European, is, on the whole, rare in the African. Small epidemics have been encountered from time to time; but its rarity, on the whole, is striking because no attempt is made to immunize the Native. This higher degree of immunity to diphtheria is reported by observers in South and in East Africa. Chickenpox and measles, on the other hand, are as common in the African as they are in the European. Tick typhus, is very rare in the Native, compared with the white man. It may be that, owing to the dark skin of the African, the rash is not easily observed. On the other hand, epidemic and murine typhus are far more common in the African Native. Mumps and whooping cough afflict the African, although definitely less often than the European.

Abortus fever is rarer in the Native than in the white man. The fact that milk is not such a staple diet with them as it is with the European, may have something to do with this.

Colloid goitre and adenomata of the thyroid are as frequent findings in the African as in the European, but thyrotoxicosis goitre, (primary and secondary Graves' disease) is certainly rare. Cretinism and myxœdema, seen from time to time in the European, are apparently very rarely or never met with in the Native. Diabetes mellitus, which is very common in the European, attacks the Native to a much lesser extent. The reason for this may be found in the differences of the diet in the two races—namely, a very high carbohydrate-low fat diet in the Native. It is said that a diet consisting of a high fat content predisposes to diabetes. Whether Addison's disease is encountered in the African is difficult to say, because of his dark skin. Pituitary dysfunctions occur, on the whole, less often than in the European.

Disseminated sclerosis, progressive muscular atrophy and subacute combined degeneration of the cord are not encountered in the Native. I should point out here that disseminated sclerosis, in the African of the West Coast, has been described; but, from the description of the cases, they may have been cases of encephalomyelitis.

Much has been written on the effects of the African sun on the European. As regards the Native, he does not appear to show in the ordinary course of events any of the ill effects from exposure, such as heat hyperpyrexia (sunstroke or heat-stroke) and heat exhaustion. These may occur in the European. Heat exhaustion is commonly seen in the coastal towns, where the humidity in the hot seasons is high. Heat-stroke is very rare today, as the European does take precautions to avoid excessive exposure, but unless he is careful he may suffer severely.

The Native has adapted himself to living conditions in Africa. He has a different coloured integument, he generally wears fewer clothes than the European, especially the primitive Native, and it is theoretically possible that his sweat glands, temperature-regulating mechanism and autonomic nervous system have undergone changes to enable him to live with impunity in the high and varying temperatures of Africa.

On the other hand, should the Native be placed in abnormal conditions of heat, he may succumb to its effects just as the European. This applies particularly to underground mining, when the temperature and humidity are high. E. H. Culver (1932) reported on 92 fatal Native cases of heat-stroke occurring in the Witwatersrand gold mines.

DISEASES MORE COMMONLY ENCOUNTERED IN THE NATIVE BECAUSE OF ENVIRONMENT

Certain diseases occur more frequently in the Native, not because his body is less resistant to them, but simply because he is more exposed to them than is the European. The Native, on the whole, knows nothing of prophylaxis. Even if he were aware of the dangers these diseases carry with them, he is not, for the most part, in a position to prevent them. Except for the periods when he leaves his reserve to find work elsewhere, he generally lives in the area in which he was born. It is of little avail to tell him to avoid rivers in order to prevent infection by

the bilharzial parasite, for he must perforce clean himself and use the water for cooking and washing. It is useless to tell him not to walk barefoot through the veld for fear of hookworm disease. The Native, on the whole, does not wear shoes. The living conditions of the European are entirely different. It is not possible to move Natives from regions highly endemic to malaria, hookworm disease, bilharziasis, yellow fever, sleeping sickness, kala-azar, filariasis and dracontiasis. Admittedly, a few settlements in the past were moved from sleeping sickness belts; but often with no great alacrity on the part of the Natives.

Typhoid, amœbiasis, venereal disease, relapsing fever, epidemic and murine typhus are much more commonly found in the Native because of his poor sanitary and unhygienic living conditions.

Nutritional disorders, which include pellagra, scurvy, beri-beri, nutritional œdema, nutritional macrocytic anæmia and vitamin A deficiency, are seen more frequently in the Native than in the European, because his diet is often very poor and he often lives in regions where the soil is poor and droughts frequent. His normal diet, which consists mainly of maize with, when procurable, a small amount of meat and green vegetables or leaves, often predisposes to pellagra and other nutritional disorders. The European diet, on the other hand, is a much better balanced one. The manifestations of these nutritional disorders are little different from those in the European, except that infantile pellagra and optic atrophy, due probably to the lack of the B group, appear to be confined to the African.

CLINICAL and LABORATORY NOTES

AN EVALUATION OF THE HUGGINS IODOACETATE INDEX TEST IN PATIENTS WITH MALIGNANT DISEASE*

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Disturbances in the blood proteins of cancer patients and in patients suffering from a variety of non-malignant pathologic conditions are often reflected in an altered thermal coagulation of the serum proteins. The test devised by Huggins *et al.*[1] makes use of iodoacetic acid as a protein coagulation inhibitor. The iodoacetate index is an expression which relates the inhibition of clotting of serum by iodoacetate to the total quantity of proteins present in the serum, and hence to the total availability of linkages essential to coagulation. Huggins *et al.*[1] obtained an index of less than 9.0 in all of 85 patients with active cancer. It was noted, however, that this altered thermal coagulation was not specific, since the index fell within the cancer range in 16 of 95 instances in patients having diseases other than cancer. In 100 normal control individuals, the iodoacetate index exceeded 9.0.

Because of the possibility that this test might be of clinical aid in the early diagnosis of cancer, we wish to report our experiences with the Huggins iodoacetate index test in a series of 200 individuals. In 135, a diagnosis of malignancy had been definitely established; the remaining 65 patients who had a variety of miscellaneous diseases presented no clinical evidence of malignancy. For the purposes of this experiment an iodoacetate index of less than 9.0 was arbitrarily regarded as positive for malignancy, while an index of 9.0 or over, was regarded as negative for malignancy.

The technique employed in the early part of this investigation was that originally recommended by Huggins *et al.*[1] A slight modification, suggested subsequently by Huggins (personal communication)* was employed in later tests. Total proteins were determined by the micro-Kjheldal method.

TABLE I.

RESULTS OF THE IODOACETATE INDEX IN VARIOUS TYPES OF MALIGNANCY

Organ involved	*Number of cases*	*Correct*	*Error*
Breast	46	34	12
Stomach	8	5	3
Colon	24	19	5
Lungs	8	4	4
Skin	11	9	2
Kidney	2	2	
Bladder	4	2	2
Prostate	4	2	2
Testicles	2	2	
Uterus	1	1	
Ovary	4	3	1
Cervix	4	2	2
Hodgkin's	3	2	1
Miscellaneous	14	10	4
Total	135	97	38

A total of 261 determinations were performed in the 200 patients. Thus, some patients had two or more determinations done at various times. Our results are tabulated below (see Tables I and II).

Our results indicate that, in our hands, the iodoacetate index test demonstrates a significant lack of specificity. There were 41.5% false positives and 28.2% false negatives. Repeated

* From the Cancer Clinic, Department of Surgery and Laboratories of The Jewish General Hospital, Montreal.

* In a number of instances, we found it difficult to establish the coagulation end point. To obviate this, a wire mesh of known diameter was employed. The coagulation end point was that degree of coagulation which failed to pass through the wire mesh after heating.

TABLE II.

ACCURACY OF THE IODOACETATE INDEX TEST IN PATIENTS WITH MALIGNANCY AND IN PATIENTS WITH MISCELLANEOUS DISEASES

Diagnosis	*No. of cases*	*No. correct*	*%*	*No. errors*	*%*
Malignancy	135	97	71.8	38	28.2
Non-malignant pathology	65	38	58.5	27	41.5
Totals	200	135	67.5	65	32.5

tests at intervals performed on the sera of 30 individuals often showed unexplained variations in the results. This lack of specificity and significant errors in both directions have been observed by Bodansky and McInnes,[2] Homberger *et al.*,[3] Pollack and Leonard,[4] Finnegan *et al.*,[5] Kiefer *et al.*[6] and Gilligan *et al.*[7] Huggins *et al.*,[1] Kiefer *et al.*[6] and Gilligan *et al.*[7] have shown that in young healthy adults, free from any demonstrable disease, the iodoacetate index rarely falls below 9.0. Patients suffering from a variety of miscellaneous diseases as well as from cancer, frequently have altered blood proteins and these alterations affect the iodoacetate index.

SUMMARY

The Huggins iodoacetate index test was performed on 200 patients. In 135, a diagnosis of malignancy had previously been established, and in this group the Huggins test was correct in 97 instances. In 65 patients with no clinical evidence of malignancy but with various other diseases, the test was in error in 27 instances. There were 41.5% false positives and 28.2% false negatives.

The Huggins iodoacetate index test appears to lack specificity as a definitive differential diagnostic test for the presence of malignancy.

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THROMBOEMBOLISM.—Successive blocks of postoperative patients, having at least 500 in each block, treated over the years since 1944, showed a constant incidence of thrombosis at about 2.5%. The first group remained in bed for a period of ten days after operation; the second group were ambulant on the first to third day; the third on the third to seventh day with the supplemental use of position, exercises and circulatory stimulation. In the final block of patients the prophylactic administration of dicoumarol caused a sharp drop in the incidence of thromboembolism to 1.5% with no embolic deaths.—J. C. McCann, *New England Journal of Medicine*, **242**: 203, 1950.

STERNAL MARROW PUNCTURE IN THE DIAGNOSIS OF MILIARY TUBERCULOSIS IN CHILDREN*

John Wilson, M.D.

Toronto, Ont.

This is the report of a study to assess the usefulness, or otherwise, of sternal marrow puncture as an aid in the diagnosis of miliary tuberculosis in children.

In 1939[1] Stahel in Germany reported the observation of a tubercle in a section made from the clot of sternal marrow aspirated from a known cause of generalized and terminal miliary tuberculosis. However, the use of this procedure as an aid in the diagnosis of miliary tuberculosis ante-mortem, was not considered until 1945. At that time Schleicher[2] of Minneapolis, engaged in investigating the frequency of tuberculosis and co-existent pernicious anæmia, found a tubercle in the gross units of one such patient, despite no x-ray evidence of an active pulmonary tuberculous process. In reporting the case, he stated:

> "It is not at all unlikely that miliary tuberculosis of the bone marrow organ may be much more common than is generally supposed. . . . With chemotherapeutic agents becoming a strong possibility, the detection of a miliary lesion by means of a sternal aspiration, particularly in those cases where chest x-ray and sputum are negative, should not only be a valuable adjunct in the differential diagnosis in tuberculosis, but should also be helpful in the evaluation of the therapeutic measures."

Subsequently,[3] he reported positive bone marrow findings in eight cases, three of which were known cases of miliary tuberculosis, and the others bearing varying diagnoses from carcinoma of the rectum to typhoid fever in whom miliary tuberculosis was not suspected. In this paper, he presented a technique for obtaining suitable bone marrow units and preparing them for examination. He reported that, from 5 to 100 gross marrow units were obtained from each case. Typical epithelioid tubercles were present in from 8 to 80% of the units examined from each patient. According to his description, such a "structure is composed of closely packed epithelioid cells. There may or may not be one or more giant cells. Some small lymphocytes and occasionally a few polymorphonuclear neutrophils are dispersed within the epithelioid part of the tubercle. A distinct wall of small lymphocytes surrounds the periphery. At or near the marginal zone of this lymphoid wall, small clusters of plasma cells and occasionally eosinophils have been noted." An occasional caseated tubercle was observed.

Anderson and Armstrong from the Mountain Sanatorium in Hamilton, in 1947,[4] reported a method of obtaining bone marrow biopsy, and processing it for histological examination. With modifications, the method was that of Schleicher, and with minor variations was used by us.

They recommend the use of a special marrow needle, which we have found useful in older children, but quite unsatisfactory for infants because of its large bore. In these latter, a No. 18 spinal puncture needle, shortened to 1½"

* From the Hospital for Sick Children and the Department of Pædiatrics, University of Toronto, under the direction of Alan Brown, M.D., F.R.C.P.(Lond.).

in length, with a short bevel, was used. The area selected for puncture was the manubrium sterni, because of the relatively large marrow centre. The skin surface was prepared with iodine and alcohol, and suitably draped. The site was then thoroughly infiltrated with 1% novocaine down to, and including, the periosteum. A period of two minutes was allowed for complete anæsthesia to occur. The needle was introduced through the skin and anterior table of the sternum by a continued rotatory motion. A sense of "give" was noted as the needle entered the marrow cavity.

A 20 c.c. syringe was then attached to the needle, and the plunger withdrawn rapidly to the 15 c.c. mark. At this point, the procedure became uncomfortable for the patient. However, it was felt that the sudden high negative pressure so produced, was responsible for the breaking away of more bone marrow units than might otherwise be obtained. Usually, in a child, it was not possible to obtain more than 2 or 3 c.c. of fluid. The syringe was then gently detached, its contents transferred to a wax-lined test tube containing 1 c.c. of heparin to prevent clotting, and the tube shaken to mix the whole thoroughly. The syringe was rinsed with normal saline, and this, too, was added.

The fluid was then poured over a No. 100 mesh wire screen to filter out the units from blood and fibrin. The units were collected by inverting the screen over a beaker, and washing through with 10% formalin in saline. They were recognized as yellowish white particles 0.3 to 0.7 mm. in diameter. Following fixation in the formalin solution, they were dehydrated by successive transfer to 50, 75, 85 and 95% alcohol. Final dehydration was effected in absolute alcohol 1:4 dioxane. Subsequently, the particles were embedded in wax, sectioned, and stained with hæmatoxylin and eosin stain.

Initially, considerable difficulty was experienced in obtaining any units by the above mentioned method. Improvement in technique was rewarded finally with consistent results. In all, sternal punctures by this method were performed on 32 children, ranging in age from three months to fourteen years, suffering from medical or surgical tuberculosis. In six of these cases, there was a miliary spread as shown by x-ray. In no case, with the exception of a fourteen-year-old girl was it possible to obtain more than a few marrow units. In none were the tubercles seen which are described by workers dealing with adults.

DISCUSSION

The problem of obtaining bone marrow units for histological study differs markedly from that of securing marrow fluid for hæmatological examination. In the latter case a few drops will suffice, whereas in the former as much as possible must be obtained. In this study, bone marrow aspirations were not done from other than the sternum. The small size of the sternal marrow centre in infants and children precludes the possibility of obtaining more than two to four c.c. of fluid. A post-mortem study of the sternal marrow centre of 24 infants ranging in age from a few hours to 2½ years, revealed that the depth of the anterior plate of the manubrium varies from 0.3 to 1.0 mm., and the marrow depth from 1.0 to 5.0 mm. The marrow diameter varies from 3 to 28 mm. The care which must be exercised in performing a sternal marrow puncture, is obvious. The use of a puncture needle of sufficient size to permit the easy aspiration of marrow units is an extremely hazardous procedure, especially in infants. Using a small bore needle sharply reduces the number of marrow units obtained. With fewer units to examine the likelihood of finding one which contains a tubercle becomes more remote.

Although, it is possible that this method of bone marrow biopsy might prove helpful in hæmatological examination, nevertheless, in our hands, it has been of no value in the diagnosis of tuberculosis, miliary or otherwise.

SUMMARY

A study of the bone marrow units obtained from sternal puncture of 32 infants and children suffering from medical and surgical tuberculosis is reported. Six cases had miliary tuberculosis as proved by x-ray. The method of obtaining and preparing the units, with attendant difficulties, is discussed. In no case has it been possible to demonstrate the tubercles described by workers dealing with adults. It is concluded that sternal marrow puncture, according to the method described, is of no value in the diagnosis of tuberculosis in children.

The assistance in this study, rendered by Dr. W. L. Donohue, Director of Pathological Laboratories, Hospital for Sick Children, and his technical staff is gratefully acknowledged.

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TREATMENT OF TYPHOID FEVER WITH CHLOROMYCETIN. —Of four patients with typhoid fever treated with chloromycetin (50 mgm. per kilo body weight initially and daily to a total of 18 to 20 gm. or until the temperature had been normal for seven days) one died within 48 hours of hospital admission from heart failure and pneumonia. In the other three temperature and cultures were normal within 72 hours. These three cases represented the acute, carrier and relapse stages of typhoid. The patient in relapse had previously been treated for ten days with chloromycetin but suffered a recurrence four days after cessation of the initial therapy with positive blood and stool cultures.—G. W. Erickson, *New England Journal of Medicine*, **242:** 177, 1950.

THE CANADIAN MEDICAL ASSOCIATION

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EDITORIAL

EDUCATION IN NUTRITION IS NOT FINISHED

SOME physicians in Canada are not concerned about nutrition, and for the lack of interest, or even apathy, several reasons could be given. There is thought to be little actual illness caused by malnutrition in this country; are we sure that is true? A considerable number of adults (perhaps 15%) are undesirably overweight, but that is not a tactful subject. Surveys have shown that large numbers of Canadian children do not receive much vitamin D. Since the textbooks say, untruthfully, that rickets is a disease of infancy only, there is not much apprehension about vitamin D deficiency. Due to a lack of undergraduate training in the subject, the knowledge about nutrition possessed by many physicians is derived from detail men and from advertising. The patient is told: "Be sure to have a good diet" and dismissed with a cheerful nod. A wide variety of special diets—most of them unnecessary and often based on personal foibles—are prescribed. Some of the diets can cause malnutrition but they are generally sufficiently annoying to keep the patient from adhering to them for long.

Despite the lack of interest there is information sufficiently reliable to warrant more attention to nutrition. Studies on children in several provinces have shown a prevalence of poor food habits and have indicated that physical signs of insufficiency can be detected. In a land of plenty there is only one real reason for faulty use of food. That reason is a combination of ignorance and indifference. The indifference needs to be stressed because reliable information is available if people wanted it. In a democratic country there is only one remedy: education.

Nutrition education is not new; it has been going on for many years and some progress has been accomplished. Certainly infants are fed more wisely than was the case a generation ago. It may be questioned whether school children are better nourished than was the practice in most parts of Canada in 1900. The general weakening of family life has had its effect upon home meals. Admittedly, education is a slow process and the general level of intelligence is such that there is a limit to what many people can learn. However, there has been a good deal of nutrition education and its effectiveness needs to be examined.

A report prepared for the Canadian Educational Association shows that nutrition appears on the school curriculum in all provinces. Has education in nutrition had any value in schools? Presumably, it has been part of general health education, and the question may be broadened. It may be doubted whether health education in schools is taken seriously. It is not an examination subject and, consequently, does not need serious attention. Can efforts in health education accomplish much if they are provided by an inadequately trained person who has never cared for children personally and who has no faith as an individual in healthful living? Children learn by doing, not by being talked at, and the time has come to enquire whether present health education is doing more harm than good by creating boredom and apathy, if not antagonism.

Education in nutrition has been impeded by confusion and contradiction. Even with so simple a matter as the amount of milk to be recommended for a nine-year old boy there is lack of agreement, and the different bits of advice have confused the public and created distrust. In Toronto it was recently observed that five different pamphlets were available for prenatal cases; these pamphlets provided markedly discordant advice. Moreover, there was too much advice in any one pamphlet to be followed easily and some of the advice was unnecessary. There is no need to tell most Canadians to eat meat; they will do so even at present prices. Nutritional advice needs to be simplified so that emphasis is given to essentials and the advice should be definite and practical. The advice should be geared to need and to the level of intelligence, and it should be accurate.

Physicians can have a powerful influence in improving food habits. No nutritional advice will be followed more faithfully than that provided by physicians. For most Canadians the best advice now available is contained in Canada's Food Rules, copies of which are readily available. Foods which are procurable in most

parts of Canada are stressed and the quantities recommended are based on sound scientific knowledge. General adherence to Canada's Food Rules in providing nutrition information would remove a great deal of the present contradiction and confusion. Special attention needs to be given to the nutritional requirements of children, of pregnant women, and of aged persons. For these three types of persons the physician can do much to provide sound nutritional advice on an effective personal basis. Such advice would be more valuable to the health of the patient than would a shot-gun vitamin prescription.

E. W. McHENRY

EDITORIAL COMMENTS

Sugar and Dental Caries

The pathology of dental caries is still obscure. The susceptibility to tooth decay is extremely high, on this continent at any rate, and shows no sign of lessening. For lack of a proved cause we have no definite point of attack. Certain facts have been established, but the significance is not always clear. For example, it is admitted that refined sugar can play a large part in producing caries. Where sugar is lacking in the diet caries is definitely less; where it is eaten in large quantities caries is undoubtedly very common; acid formed in the breaking down of sugar in the mouth can dissolve the tooth structure; some degree of control of caries is possible if either (*a*) fermentable sugars are eleminated from the diet, or (*b*) are prevented from being broken down to acids, or (*c*) if the acids are removed or diluted before they can act on the tooth.

A large body of circumstantial evidence can thus be built up to incriminate sugar.* But it still is circumstantial and there are other facts to be accounted for. Caries can occur in the absence from the diet of concentrated refined sugar, as amongst primitive peoples; it does not occur in all those who do eat sugar; experimentally, the action of the acids found in the mouth from fermentation does not produce the typical carious lesion seen in ordinary life; it is disputed whether the source of the acid is sugar or organic material.

We need more facts to understand fully why caries occurs, and these must be set in proper relation to each other. To blame it all on sugar is a tempting conclusion, but one which has yet to be proved.

* For a very full discussion of the subject see: Sugar and Dental Caries: A Symposium; *J. Cal. State Dental Assoc.*, **26**: No. 3: 1950.

The Association of French-speaking Physicians of Canada

We welcome the full account by Dr. Seguin, our Quebec correspondent, of the recent meeting of the Association of French-speaking physicians of Canada in Montreal (p. 516). The meeting showed evidence of careful planning, and the link with France was most effectively maintained by the official delegates, Professor R. Kourilsky and his wife Dr. S. Kourilsky. Dr. S. Lamotte-Bourillon of the medical faculty of Paris was another distinguished guest.

The program was specially designed to interest general practitioners, dealing as it did with the most lively topics of the day in medical economics, together with papers on antibiotics, on diseases of the respiratory system, and by Dr. Hans Selye, on cortisone and ACTH. One session was devoted entirely to problems of the general practitioner; his difficulties in following his patients after their admission to hospitals in large centres; and his lack of facilities in remote country districts. The difficulty in getting doctors to work in such districts, as was suggested, can be best overcome by giving them better diagnostic and hospital facilities, to organize meetings and postgraduate teaching by the co-operation of medical societies; to make university teaching itself more objective, that is, less specialized and more clinical; to allow students the opportunity to be associated with country practitioners. The help of governmental agencies should be invoked to work out these matters.

MEN and BOOKS

OLD TIMES IN MEDICINE*

A. G. Morphy, M.D., C.M.†

Dorval, Que.

I began the study of medicine at McGill University in 1886, and when I had got through the preparatory subjects, anatomy, histology, botany, physiology and chemistry, I went down to the Montreal General Hospital for my first clinic. Built of grey limestone darkened by age, it was situated in a thickly populated part of the city, near the docks and factories. Externally it might have passed for an Orphans' Home, but once inside no mistake was possible. The smell of ether and iodoform and other matters hit me in the face.

In the medical wards, among the average lot, were patients with open pulmonary tuberculosis, with sputum cups on their bedside tables. True, Koch had isolated the tubercle bacillus in 1882

* An address delivered at the June, 1949, staff meeting of the Veterans' Hospital, Ste. Anne de Bellevue, Que.

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but his researches had apparently not yet proved it as the cause of the disease, and consequently no precautions were taken. And there were patients with typhoid fever, more in the late summer when the water in the St. Lawrence River was at its lowest yearly level. The water was pumped directly, without chlorination, into the city mains and reservoirs. The bacillus typhosus had not been discovered. Milk was also a source of infection through hands of milkers and cans washed in plain water.

My first visit to the operating room was an event. The ceiling was low, the air thick with the fumes of ether and the odour of iodoform and the exhalations of a crowded amphitheatre in a comparatively small room. There was little ventilation, and I had to hang on to my dinner. The operating surgeon and his assistant had taken off their coats and rolled up their shirt sleeves and wore rubber aprons. They had scrubbed their hands with soap and water and soaked them in a solution of bichloride of mercury. The instruments lay in dishes of carbolic solution. On the wall near the operating table hung two large glass jars, one containing bichloride, the other carbolic solution, each with hose attached for irrigating the surface about to be cut or the wounds made by the cutting. Lister's carbolic spray was not used, for the air was not held responsible for infection. It is noteworthy that Lister's adoption of antiseptic methods had preceded the period of which I write by only fifteen years, and now the pre-antiseptic time when operations were followed by suppuration, pyæmia and the dreaded hospital gangrene, seems part of the Dark Ages.

In the Montreal General ether was the anæsthetic generally used, chloroform only in exceptional cases. Into a cone covered with thick cloth, with a lump of absorbent cotton inside, you poured a good lot of ether, clapped it on the patient's face and wrapped a small towel about it to prevent extra air from getting in. The patient would struggle for air, but you were advised to give him a breath as rarely as possible. And when he ceased struggling and the eye reflex was gone, he was well under and you nodded to the operator to go ahead. A crude method, but effective.

In comparison with the present time, the scope of surgery sixty years ago was very limited. Opening the abdomen was still a very serious matter, for not many years previously it had been followed in many cases by death.

Gynæcology, a branch of surgery, was comparatively new and perhaps looked down upon by the older surgeons. Here is a little episode: The late Dr. Roddick, a big burly Newfoundlander, has just about finished his operation and remarks to the students. He goes into the anteroom and drags in the late Dr. Gardner, a small soft-spoken man, a pioneer gynæcologist, with the words "Come in, Gardner, and let us show you some *surgery*."

Appendicitis as such was at first named typhlitis, or inflammation of that portion of the gut from which the appendix springs. In my pre-medical days I can remember people dying of "inflammation of the bowels" who in most cases doubtless had appendicitis. By 1890, or perhaps earlier, appendicitis had been clearly demonstrated, and if spotted in time, was followed by operation and recovery.

Of brain surgery there was practically none beyond chiselling a piece out of the skull to relieve the pressure of a brain tumour, or if a brain abscess could be located, to drain it. Local anæsthesia had not come into practice, and prolonged administration of ether might be followed by pneumonia. In the absence of x-rays fractures were set by observation and by measurements. In obstetrics Cæsarean section was resorted to only very rarely, in fact only when it was deemed impossible to deliver the child through the vagina. In my medical course I never saw one. Nowadays it is frequently practised.

I find it difficult to carry my mind back to the time before the invention of the incandescent electric light for "scopes" of different kinds. In old days a skilled eye or nerve specialist, if a gas light or a lamp was not handy, would light a candle and possibly hold it himself while he used an ordinary ophthalmoscope, and that was some trick.

In the wards the medical and surgical clinics were conducted on the Edinburgh method, namely ten or twelve students standing about a bed containing a patient, a professor or his assistant demonstrating the case and asking the students, one by one, to examine the patient under his direction.

This method, I have been informed, had been introduced into McGill by Osler and Roddick. In contrast to the old plan of lecturing on a patient to a class of sixty or more students in an amphitheatre, it proved of enormous advantage, and in this respect if not in others McGill's medical course was distinguished.

Sharp and accurate observation were part of our training. We had no x-rays to depend upon. Diagnoses were made by physical examination and by the patient's history. In abdominal conditions especially much stress was laid on the sense of touch. "An eye on the end of your finger" was an old saying. And in chest conditions an acute sense of hearing was essential. Only in recent years had the binaural stethoscope come into use. I recall a ward in the Vienna General Hospital in 1902, the "Assistent" examining a patient's chest with the old single wooden tube stethoscope invented by Laennec, putting it aside and applying his ear direct. Our predecessors in England carried them in their plug hats as Conan Doyle pictures his friend Watson doing, and, to complete the allusion, Doyle spotted him as an M.D. also by the smell of iodoform and the stain of nitrate of

silver on his fingers. Nowadays an M.D., if not carrying a bag, looks like a business man with a medical aura. I have noticed when attending medical conventions that the M.D.'s are a rather serious looking lot.

For diphtheria before the days of antitoxin the only treatment was tincture of perchloride of iron given internally and swabbing the throat with some horrible mixture, a proceeding I found distressing when I applied it to struggling young children. A child with laryngeal diphtheria choking to death is a sight reserved for me in hell if I ever get there. The name of the New York doctor who spent much of his earnings in tubes made of gold or platinum to be inserted into the larynx in these cases I have unfortunately forgotten. He was a benefactor and his method of intubation saved many lives. The difficulty for doctors in small towns and in the country remote from specialists was that special skill and apparatus were required to insert the tube, and for lack of these many children died.

Then came antitoxin. With doubt and hesitation I injected 500 units into a girl aged fourteen who had been ill three or four days, and she died. My state of mind was unpleasant. Had I killed her with this new remedy? Later, experience taught me that I should have injected at least 2,500 units as soon as I had diagnosed diphtheria. "Experience teaches but the fees come high."

For diabetes the treatment was mainly reduction of carbohydrates to a minimum, and as the pancreas was under suspicion pancreatin was given on trust, but unsuccessfully. A most pathetic case of a little girl starved in this way, begging, even praying for a piece of cake or a slice of bread with jam on it I shall never forget. She was not my patient. Her mother was. If she'd been mine I'd have given in, be the result what it might. She died later.

For syphilis the chief remedy was mercury preferably in the form of ointment rubbed into various parts of the body, a new spot each day for six days and a bath on Sunday, and then on Monday begin again; and look out for salivation. Iodide of potassium was also used. Courses of treatment each lasting three months had to be continued with intermissions for two years before the patient could be considered cured. And even then, years later, general paralysis might follow. There was no cure for that. Wassermann had not discovered his famous reaction nor had Quincke presented lumbar puncture to the medical world. When salvarsan (606) in its crude form came into use I injected some of it into a woman patient. Her face and hands swelled up immediately, she turned pale, her pulse became weak and I feared she would die on the spot. It was a bad moment. Fortunately for my peace of mind at least, she did not. It was powerful stuff, kill or cure.

In pneumonia we depended upon good nursing, digitalis, quinine, whiskey, hot poultices to the chest, and trusted to the grace of God and the patient's resistance for recovery. I'll never forget an old Irishwoman dying of pneumonia, aware that her last hour had come. "Doctor", she said to me between short breaths, "now you've done all you can, so call in the Rev. Mr. H. and he'll see me safely off". Humour to the very last. A brave woman.

In those days there were no "wonder drugs'. Many patients died of acute infections who nowadays would have been saved, and doctors had to stand by, helpless, and see them die, their only consolation being that they had done their best with all resources available.

In my medical course the lectures on obstetrics were given by the late Professor J. C. Cameron. He was fluent, his descriptions graphic, he demonstrated with his hands and fingers as he talked, and he captured one's interest. But while the theory was plainly set forth practice was deficient, for the old Maternity Hospital was small and the opportunities of witnessing actual child-birth were scanty. A four year student was lucky if he had seen more than three births. In my own case in my early years of general practice in Lachine I found that there was hardly any emergency that made me "sweat blood" so painfully as a difficult obstetrical case, with no skilled help available, generally between midnight and four a.m. The only thing to do was to cast fear to the devil, call on my resources of theoretical knowledge and native ingenuity and go ahead, the practical nurse or neighbour woman volunteer help or even the husband giving chloroform under my direction.

Should any harm result, and the baby's head be injured by forceps when a narrow pelvis or over-sized head necessitated strong pulling, even though tempered by caution, I had to bear the brunt of criticism, but that was all part of the game of life. I never liked that line of Longfellow's, "Life is real, life is earnest". By contrast Tennyson makes Ulysses allude to his mariners as "souls—that ever with a frolic welcome took the thunder and the sunshine". And so the young M.D., up against similar or other difficulties either works out, unconsciously perhaps, a philosophy of life or sinks under it. But if he has guts he won't sink.

In this connection the following case, though not very difficult, may prove of interest.

On the shore of Lake St. Louis, an expansion of the St. Laurence, opposite Lachine, lay Caughnawaga, an Indian Reserve, a collection of wooden cabins in the midst of which towered a stone Roman Catholic Church. The inhabitants were half- and quarter-breeds, Iroquois, with a mixture of French-Canadian and Scotch, the latter inherited from the Highland Scotch troops sent to Canada in the wars of 1775-6 and 1812-13 to repel invasion by Americans, and some of the Scotties had married squaws and settled down and raised families.

A C.P.R. single track bridge a mile long spanned the lake. On it was a notice "trespassing forbidden" but

this did not deter hardy Caughnawaga men from walking over it six mornings a week and back in the evening in winter time or when the lake was too rough for paddling over. They worked in the Dominion Bridge Company's shop at Lachine. A girder a foot wide ran along beside the track, leaving a space of about a foot and a half between your knees as you sat on it and the wheels of a passing train. Or, if you preferred you could turn your back to the train and let your legs dangle over the lake forty feet below and meditate on your sins. Either way I found a trying experience when I accepted a call to Caughnawaga.

In my early years of practice a notorious Caughnawaga man was Big John Canadien, generally known as Big John. It was his custom for many years to paddle down the Lachine Rapids on the south side in a large canoe with six expert paddlers each New Year's Day, a feat requiring skill, daring, and courage. I've never heard how much "firewater of the paleface" was drunk afterwards, but I happen to know that the law forbidding sale of liquor to Indians was enforced, let's say, irregularly.

One very cold night in February, temperature below zero, a ring at my door-bell wakened me.

"Who's there?" I asked from my bedroom window.

"It's me, Big John."

"What do you want, Big John?"

"Young woman over there try to have baby and can't do it. She want you."

"I'm not going to walk over the bridge tonight, there's big wind blowing."

"You no walk. I fix that."

"How can you?"

"Doc, you know me long time, I fix it."

"No, I'll not go. It's too cold."

"Maybe she die, Doc."

That settled it. "All right."

I dressed very warmly, fur coat, cap, and sash, saw that my obstetrical outfit was complete and toddled along.

Big John and I walked to the edge of the river, then a hundred yards on the ice to a point where a boat was drawn up on it. The sky was dark and cloudy. No stars shone, and the swift-running water of the mighty St. Lawrence looked black and cold. A thrill of fear ran through me as I thought of my wife and daughters. Big John, stolid half breed, pushed the boat into it and held it.

"Get in, Doc."

He shoved off and jumped in, rowed a few yards pointing the boat upwards against the current, dropped his oars, hoisted a sail, and steered with a paddle, shifting it quickly from one side to the other as the direction of the boat altered, and slacking or tighening the sail rope according to the force of the gusty wind. And then, to my surprise, he lit his pipe just as if we were sailing easily in calm weather.

Arriving at the other side we walked again over a hundred yards of ice and then to Pete's cabin.

On the bed lay young Marie in labour with her first baby, and beside it sat Pete, helpless, trying to console her. Four or five half-breed women in black shawls sat expectantly against the walls, and the village midwife informed me that the pains had begun twenty hours back, and "the baby not come".

Having scrubbed hands and arms and soaked them in antiseptic solution, I made my examination. It was a breech presentation. I pulled a tiny foot out into the world. The women gasped. They were Catholic.

Pete, nearly heart-broken, had gone to his mother's cabin.

"Is there danger to the child?" was the question.

I knew what to do. Friends had told me. I baptised the foot solemnly and with a solemn feeling,—for I respected their belief,—with water out of a cup. My being Protestant didn't matter. Their relief was intense. In a few minutes the baby was born. A moment of anxious suspense while I held it up by its feet and gently slapped its back. Then the little shrill cry and the women babbled with joy. In good time the Curé came and thanked me for my timely services and shook hands.

On the way home the wind had abated and Big John had to row all the way across the mile-broad river.

Very troublesome cases in my early practice were babies with what I regarded as milk poisoning. We would now label them bacterial enteritis. When all patent foods or barley water or even boiled water were rejected and the diarrhœa persisted, I was "up against it". The baby would soon die. Nowadays we could run nourishment into a vein and save the little life, but not then. Some died, despite all my efforts. One that survived I remember very distinctly. Its mother had gone away for a few days leaving it to the care of a maiden aunt. All foods even in very small quantities were rejected. Then came a brain wave. I told Auntie to half-cook a piece of juicy beefsteak and give it and a crust of bread to the baby to suck. It recovered, and Auntie could sleep o'nights.

Medical education did not (does it now?) include teaching the young doctor discretion, even tenderness, in his attitude toward dying patients. In himself he no doubt possesses these qualities but in his regard for strict truth he may forget to exercise them at a moment of such supreme importance, with his patient about to enter the valley of the shadow of death.

The following experience made a deep impression on me.

Jacques Leroux stood at the door of his butcher shop smoking a pipe of tabac Canadien. He was of stocky build, well nourished, about 35, and apparently indifferent to everything but his business and his own comfort. The English and Boers might kill each other off for all he cared, and as for politics, he voted for Laurier and left the matter at that. And for the sake of his soul he went to mass regularly every Sunday morning.

There was one trouble, however. His wife was sick. And as far as he could worry about anything outside of poor business, he was worried about her. They had been married fifteen years and she had brought him no children. That was bad, but, he maintained it wasn't his fault. She was a woman of good size across and rather tall, but he concluded there must be something wrong inside. And he left the matter at that, for, he said with a shrug, "I am not docteur".

He had heard of a new doctor in the town, English, and of good repute. So he called me, to see what I could do. I walked up the narrow stairs leading to the living rooms above the shop.

In the front room lay a woman propped up on pillows, breathing hurriedly, her cheeks flushed with fever, her pulse running fast. She was very thin, and her large black eyes looked imploringly at me, as if to say "You are my last hope". Even without examining her chest I knew that she was far gone in tuberculosis, but I examined her just the same.

She must have seen the grave expression on my face, for she asked (in French) "Am I going to die, Docteur?" I nodded. Her black eyes flashed fire, she sat up in bed and cried "But I must not die, I cannot die. You want to know? My husband will marry the servant girl right away. He will not wait. I know."

She fell back exhausted. I tried to console her even a little, but could not. I'd finished her. I went down stairs and told Jacques who merely shrugged and said "It is the will of God".

According to a report which reached me later, Jacques and the maid paraded before the Curé the day after the funeral and requested him to marry them. The Curé declined, stating that Jacques must wait twelve days. So at the end of twelve days they two were wed, and Jacques stood at the door of his shop wearing his stained apron and smoking tabac Canadien, same as ever. Let us be charitable and say that he was not heartless but philosophical.

I would like to pay a tribute to the volunteer practical nurses who assisted me in my early years of practice. They had no knowledge of medical treatment beyond simple old fashioned remedies such as senna "tea", or camomile "tea" as a soothing draught, castor oil, patent cough mixtures, mustard plasters and so on, but they were faithful in carrying out the doctor's directions. They worked as many hours as were required, and they were careful to make their patients as comfortable as possible. They were not obsessed with keeping a chart accurate and spotless in black and red, the patient being "the thing", and in my experience they never put cold sheets direct from the laundry on a patient's bed. These were "aired" at the kitchen stove. They thought of the patient herself or himself, and in this respect they were ahead of their time.

Sixty years ago the science of medicine rested on a solid basis of pathology, in essence materialistic, while treatment of disease was largely traditional, based on experience and only partly on experiment. Bacteriology was in its infancy. Mind and body were separate entities. The concept "disease" overshadowed the concept "individual" and the concept "organism-as-a-whole" had not been born, nor its recent follower "psychosomatic medicine" which is now fashionable and may run to extremes before the whirligig of time brings it down to a rational level. Dr. William A. White (20th Century Psychiatry) writes "every illness has its psychological component". It is remarkable that wise old family doctors knew this, dimly perhaps, but beyond question they did and made use of it. It is heartsome, in this age of specialism, to read of the recent movement to resurrect the general practitioner whose concern is the whole body and who, if he knows anything about life outside of medicine and has a steady head and broad sympathy, becomes the family's philosopher and friend. While the parson is received more or less formally in the parlor, the doctor works more intimately in the bedrooms, and in poorer families may have occasion to go to the kitchen.

But now comes in the social worker. She has probably had a course in psychology which is all to the good provided she has basic common sense. Has she, though, the comprehensive view of the experienced family doctor whose mind has been disciplined by his medical studies and possibly by the reading of history or philosophy or the classics in fiction?

In psychiatry half a century ago old ideas held firm as rocks that don't melt in the sun. There was no treatment, only custodial care and in some disturbed cases restraint. No occupation therapy as such, but certain patients allowed to work. In præcox the outlook was poor or bad, in the manic-depressive psychosis some patients recovered, for such was its natural course. In general paralysis, paralytic dementia, the outlook was hopeless.

MEDICAL ECONOMICS

MEDICAL SERVICES IN GREAT BRITAIN

Harris McPhedran, M.D.

Toronto, Ont.

"Oh to be in England
Now that April's there."

These lines would suggest that there was a longing to be in England and that April would be an ideal month to be there—weather warm, grass green and flowers in bloom. About the longing, there was no doubt. We had it. But as to the warm weather, there was a disappointment in store, as we ran into a snow storm in Scotland and the South of England had 4 to 5" of snow. But the cold, inside homes and offices and out-of-doors was offset by the warm welcome given by all.

Leaving Malton Air Port at 9.45 a.m. on April 20, we arrived at Prestwick at ten o'clock the next morning. The sun was shining, the air cool. It was heartening to have an airport stewardess come aboard our plane and in a modulated voice say to the passengers: "Good morning, welcome to Scotland" and then proceed to give in detail where we were to go and what to do to get by customs and immigration officials. That evening, we proceeded to Edinburgh and were welcomed by Dr. Walker, Secretary of the Scottish Division of the British Medical Association, who outlined to us his plan for getting a look at the working of the National Health Scheme in Scotland and England. According to his carefully worked out schedule, we were in for a busy time and such it proved to be.

A practitioner of medicine for over thirty years, I had been authorized by the Canadian Medical Association to stay in Great Britain from April 21 to May 8, on my way to Australia, (Altogether 16 days—16 weeks would have been better) and glean all information possible about the National Health Scheme and its bearing on the practice of medicine, especially general practice. With that in mind it was determined to make a spot check of the views of civilians, specialists, and general practitioners, health officers, and others, a miniature Gallup Poll in Scotland and England.

Said one Glasgow workman, with a hearty guffaw: "Ho! Never had so many bottles o'

medicine in me cupboard in me life. And if I was really sick I'd be dead standin' in the queue, before I'd see me doctor!''

A travelling salesman: ''My doctor sent me to an outdoor clinic. They kept me coming back and coming back. Finally I gave up and went back to work. Decided to put up with my disability.''

An attractive young woman of good middle class background: ''I wasn't feeling up to par and went to our old family doctor for a 'check over'. He was too busy. He refused to examine me, and gave me a bottle of medicine. I was furious. I wouldn't take the old medicine. And I haven't gone back. I'd like to find a doctor whom I can pay myself.''

A business executive: ''I know I should see my doctor, but I've done nothing about it. I don't want to queue up, and I'm too independent to ask for the favour of a special appointment.''

A bright young business man: ''I speak feelingly. My father's very ill right now. We need the doctor often, and sometimes at night. Under the old system, when we paid him direct, our doctor would come willingly any time. Now we feel it is an obligement when he comes. We don't like asking him to come.''

A thirty-year old waiter in a restaurant: ''I think it's a great thing for the country. My wife had the same eye specialist as the Queen. My children are getting attention that we couldn't afford before. Isn't it right, sir, that if our country's worth fighting for, it ought to have these things in time of peace?''

An intelligent waitress, in a lilting Scottish voice: ''It's a great help to the working people, sir, and that's a very good thing, isn't it? I have two children, and now they get to the doctor when they need to.''

General Practitioners

One in a country district, serving a large area in co-operation with her husband, said: ''I have no time for reading or recreation: forms to fill, letters to write and medicines to dispense—all after my evening surgery and calls are through, make life one round of work and no let up. My husband and I can't take a holiday. We can't afford it. If we get a locum, we have to pay him out of our own pocket, provide him with a car and his living. We can't do it. We can't attend our patients once they enter hospital and so lose contact with them. Our most demanding patients are those who formerly paid their bills. They expect us to examine and prescribe for them and then spend some time, thereafter, socially. Some expect us to arrange for ambulance as well as bed in hospital. This takes time—telephone calls, etc., and if this is not done, we may lose them from our panel. Doctors now are like the green grocer. We are called on the telephone by patients and requested to send this, that and the other thing which they want. We are rapidly getting back to the status of doctors 100 years ago when they went in the back door. Even with my poor brain, I could not have created a worse scheme of things for the general practitioner than the present one. I would not let my young son be a doctor. We can't even afford to go to this coming annual meeting of the British Medical Association.''

In a large industrial area, a general practitioner told me he saw 40 patients at his morning surgery, made 25 calls and saw another 40 patients at his evening surgery. His financial status was improved, as he was now being paid for service to people who in other times paid little or nothing, but the work involved was too heavy and panels were too large to give adequate medical care, as most of them needed attention of one kind or another.

In another place, these opinions were voiced: ''Practitioners are being separated into two groups—specialists and general practitioners—the former working almost exclusively in hospitals and the latter in homes and offices. This is bad for both general practitioners and specialists. It is degrading for general practitioners since they cannot follow their patients into state hospitals, and so they are out of touch with them and their illnesses, while they are in hospital. All this in the days of psychosomatic medicine. Also, they cannot consult with the specialists who treat their patients, even though in a preferred position to give him the family background, social conditions, etc. Moreover, there is no opportunity to talk with specialists and be brought up to date with advances in medicine. This is a great loss to those in the front line of practice. Patients and doctors tend more and more to be just cogs in a machine. Doctors all seemed to be overworked and the general practitioners underpaid according to the services rendered.''

Country practitioners suffer a further handicap as they cannot possibly have on their panel a sufficient number of persons to give them an adequate income. In an effort to correct this and help them out financially, the government has given them a mileage allowance, but this does not compensate for more work, more driving and unreasonable demands on time and energy for ailments which two years ago patients would either ignore or come for advice to the surgery. It was thought that a direct charge to the patient for his medicine or for the first call would have a salutary effect.

I think it should be mentioned that in residential areas where the family physician could hardly make a living under the N.H.S. *some* families had remained *private* patients to help him out.

Also many who *could* remain private went on the scheme because of the money they were paying every week to the government. They con-

tinue seeing specialists and feel disgruntled that they pay both ways. Cannot even get their medicine "free".

SPECIALISTS

A great majority of the specialists interviewed were unhappy. Specialists working part time in hospitals and part time in consulting work, were especially dissatisfied. One such who works on till the late hours of the night said, "The scheme is leading to complete demoralization of both doctors and the people. It is a bad thing to create in the minds of people the idea that anything is 'free'. I am overworked and while my income is about what it was before the Act came into effect, I see more people and have less time for reading and recreation than ever before. It is bad as far as I am concerned, from every standpoint. The out-patient department is overcrowded, the complaints of patients are all too frequently trivial. General practitioners tend to unload their patients on the hospital's outdoor."

A professor of surgery stated that many of his patients wanted private beds, were willing to pay for such accommodation, but there were few private beds in the large hospitals and he could not charge the patients who chose this accommodation over 50 pounds, although they were able and willing to pay more than this amount. Nursing homes were being forced out of business by increased overhead and shortage of nurses so his income suffered further from this handicap. He said the scheme placed physicians rather than surgeons in the saddle. (This, of course, is as it should be!)

One highly placed physician doing part time work under the government plan said he belonged to a fast disappearing group, as those following after him might well be whole time government servants. He doubted the wisdom of this. It tended to an increase in an impersonal attitude of doctor to patient and drove the wedge between the family doctor and the specialist. A patient thus tended to become a cog in a coldly scientific, official machine.

Another highly trained and highly placed physician said he was an out and out socialist and thought a complete revolution in the practice of medicine, as brought about by the National Health Act, was the only way a change could have and should have been effected. He was the only doctor who expressed such an opinion.

Nowhere did I hear any doctor complain of direct government interference between himself and his patients.

PUBLIC HEALTH SERVICES

Adequate uniform diets for all people which began during the war are being continued. Seldom, even in the poor districts in cities, did I see on the streets starved or ill nourished children.

It was my impression that the pre- and post-natal care of mothers and the supervision of children was much better under the Act. One good general practitioner thought that expectant mothers could and should arrange to stay home for their confinement and thus ease the load on hospitals. He admitted, however, that present economic conditions and the desire to have a specialist were potent factors in patients deciding to go into hospitals, and by-pass the family doctor.

One conscientious general practitioner in Edinburgh (who kindly allowed me to sit with him in his office during his evening surgery) said (when a father came to him for cough medicine for his adult son) "This young man has bilateral pulmonary tuberculosis but I cannot get him into hospital or sanatorium. The former will not and the latter cannot take him—no beds. All I can do, under the circumstances, is to try and get extra food for the patient and give him medicine to control his cough. You can imagine what the result will be in this family. Multiply this situation 10,000 times and think of the result in this country."

(In Scotland alone it is estimated there is a shortage of 1,600 beds for cases of tuberculosis—*Brit. M. J.*, July 8, 1950).

NURSES

Nurses, in spite of the fact they are paid while still in training, are far too few and at the end of a two years' trial of the present scheme they are not coming forward in adequate numbers. One graduate nurse, to whom I talked, could give no explanation of this except the indifference of young people to this or any other kind of work. She thought, however, the status of the nurses had been improved not only because they were paid while in training but because they could now devote their time to nursing rather than to pleasing the private patients of doctors on the hospital staff with tea and sandwiches. This same nurse also said that the patients from the middle income group did not seem to mind being in a large public ward with the lower income group, as they felt any incidental discomfort was offset by care at the hands of specialists.

HEALTH CENTRES

I was informed that Health Centres, as a pre-election promise of the government, have not, with a few exceptions, materialized. Materials to build such are lacking and even if available, the cost of construction would only add further to the over-all cost of medical services which have risen from an estimated £167,000,000 in 1946 to £600,000,000 pounds, for 1950-1951.

HOSPITALS

Hospital beds are in short supply. "It will take a long time with building restrictions and lack of materials to overcome a shortage which the government should have anticipated. There has been the inevitable rush of patients to hospitals. Both these the government should have anticipated. All government hospitals have highly qualified, appointed, paid staffs, full-time or part-time. This has had one good effect as it has kept unscrupulous, inadequately

trained doctors from attempting surgical operations which they cannot do, or are unnecessary, and undertaking other treatments (*e.g.*, for diabetic coma) which should be under the supervision of experienced, skilful physicians, and in hospital.

Red tape interferes with getting equipment. The head of one large hospital department told me he got the equipment first and the authority after. "They will not take it away from me once I have it."

REGISTRARS

What of the recent graduates? There has been an increase in those who want to be specialists. This is largely economic in origin, as a specialist is better paid and his future more secure if he gets a hospital or university appointment. But here is the rub. Large numbers of Registrars (our Residents) are now finding there are no openings vacant in state hospitals and after long years of training to qualify as specialists of one kind or another, they cannot get a hospital post and will have to go into general practice. I think there is nothing regrettable in this, having long held the view that every specialist should have had experience in general practice which broadens his interest and outlook and sympathy for those men who are or intend to make general practice their vocation. It will, I hope, destroy the tendency of specialists to consider themselves a superior group looking down their noses at the "poor" general practitioner who after all is and should be the key stone of any system of practice—the all round specialist, requiring a wider knowledge of all branches of medicine than those who confine their training to any one specialty. Team work is essential for the full application of advances in medical science. The services of general practitioner and specialist are essential and complementary.

The war against disease cannot be won without the complete co-operation of all concerned.

SUMMARY OF BENEFITS AND DEFECTS

BENEFITS

1. People who ordinarily delayed going to see a doctor because of the cost now feel free to consult him early about their symptoms.

2. Those formerly insured under Lloyd George's scheme, now have medical care assured for their wives and children.

3. The lower income group can now obtain, without direct cost to themselves, expensive medicines, appliances, etc. This is a great boon which has unfortunately led to rather widespread abuse. Rebecca West lays stress on the fact that this class has always been well cared for medically. This is true, but may I ask at whose expense this care was given? The doctors mostly. The writer is happy to see that burden lifted from the shoulders of the profession even though the recipients now seem to be on the way to ruin the whole scheme through ignorance and greed. One hopes this is a passing phase.

4. Preventive services made effective through instruction of mothers regarding their own and their children's health are good and I was told are producing encouraging results. This is the fundamental factor in any health education program.

5. Nearly all general practitioners are now debarred from the hospitals. Much as this may be deplored, there is some compensation in that it prevents unscrupulous general practitioners from attempting surgery that may be legitimate but is often unnecessary.

6. Regional doctor committees can keep young doctors out of over-serviced areas. This is good if these young doctors can make a living elsewhere—on the whole, however, I do not like such regimentation unless the Government sees to it that they can live reasonably well and have every facility for sound practice in another less favoured place. Some provision has been made for this contingency, but to me it seemed inadequate.

7. The number of young men and women applying to enter medicine has not diminished. Those I saw in one clinic seemed well up to the quality of former groups and aware of what was facing them. I asked one bright young house officer what he intended to do and unhesitatingly he replied "General Practice". He seemed happy in and proud of his vocation.

DEFECTS

1. Doctors are overworked and underpaid especially general practitioners who have little time for reading, recreation and postgraduate courses even though the latter are now becoming available again.

2. Overwork means little time for history taking (the main factor in arriving at a diagnosis) and physical examination.

3. Payment in full or part, of hospital medical staffs leads to an impersonal attitude towards patients and this in the days of psychosomatic medicine—this is not, of course, universally applicable. It applies to 1 in 12 of doctors probably, but enough to give the service a bad name.

4. The Act has caused an almost complete division of the profession into general practitioner and specialist groups who have little contact with one another. This is bad for the science of medicine.

5. Abuse of the benefits of the scheme arises because there is no restraining direct charge on patients, too many of whom tend to make unreasonable demands on doctors' time and energy through emergency and unnecessary calls at the surgery or into the country. This is done, I am sure, by an unthinking minority. Many (all too many) make unreasonable claims for drugs, dressings, appliances, hospital and ambulance service.

6. The cost has become prohibitive: it has more than tripled since the inception of this scheme.
7. The government has moved too fast and gone too far at one fell swoop.
8. Many who are "just not well" hesitate to seek advice for themselves as they know their doctor is overworked.
9. An intensive educational course for both profession and people should have preceded introduction of the Bill.

(A subsequent paper will deal with lessons to be learned from National Health Services in England and their possible influence on similar legislation in Canada.)

ASSOCIATION NOTES

Annual Meeting, Montreal, June 18 to 22, 1951

Arrangements for the annual meeting for 1951 are well under way. The program is to include coloured television, for the first time in Canada, and the general pattern of the papers and conferences will be designed with the needs of the general practitioner continually in mind.

Mount Royal Hotel, Convention Headquarters

Details will be published each month. Meanwhile members are urged to make their reservations early. Use the form shown on next page.

HOTELS	RATES		
	Single	*Double*	*Suite*
Mount Royal (Convention Headquarters)	$4.50 up	$7.00 D.B. up 8.00 T.B. up	$14.00 up
Windsor	5.00 up	7.00 up	15.00 up
Laurentien	3.50-$5.50	6.00-$9.50	11.00 up
Queen's	3.50 up	7.00 up	9.00 up
De LaSalle	4.00- 7.00	6.00- 8.50	9.00 up
Berkeley	4.00 up	7.00 up	11.00 up

(All above rates include bath)

MEDICAL SOCIETIES

Le XXe Congrès des Médecins de Langue Française

L'omnipraticien était à l'honneur au XXième Congrès de l'Association des Médecins de Langue Française du Canada, tenu à Montréal en septembre dernier. En effet, par la nature même des sujets traités, de l'hygiène et de la médecine préventive, en passant par les indications et contreindications des antibiotiques jusqu'aux questions les plus pertinentes d'économie médicale, tous les rapporteurs, pour la plupart des spécialistes, avaient préparé de nombreux et intéressants travaux pour l'édification de leurs confrères praticiens.

Il était inévitable aussi qu'à de telles assises la France délégua quelques-uns de ses plus dignes représentants, notamment dans la personne du professeur Kourilsky grand ami des Canadiens, car elle ne pouvait rester indifférente aux efforts d'un groupement resté si fidèle à la culture ancestrale.

Elève de Sergent et spécialisé lui-même dans les affections des voies respiratoires, le professeur Kourilsky fit part d'une importante communication jusqu'ici inédite. Elle avait trait à la primo-infection tuberculeuse affectant d'emblée le complexe gangliopulmonaire. Au moyen de la tomographie, on reconnait aujourd'hui que c'est dans le ganglion qu'aboutissent la plupart des bactéries, quelques-unes seulement s'arrêtant au passage dans les alvéoles et provoquant simultanément un foyer initial d'alvéolite. Avec de nombreuses preuves à l'appui, le rapporteur démontre que plutôt que par voie d'inhalation, comme on l'avait toujours cru jusqu'ici, la primo-infection tuberculeuse pulmonaire se fait par la voie digestive, non pas avec les aliments mais davantage par la contagion digitale, chez les enfants notamment mais aussi bien chez les adultes. Dans une autre leçon sur l'asthme, le professeur Kourilsky dit que contrairement à l'Europe où le facteur nutritionnel est en cause, ici au Canada c'est notre climat qui par sa rigueur et ses transitions débilite nos voies respiratoires.

Une autre communication fort goûtée fur celle que prononça le professeur Hans Selye, Directeur de l'Institut de médecins et de chirurgie expérimentale, à l'Université de Montréal. Il donna des précisions sur sa théorie du "syndrôme général d'adaptation", et comme quoi il importe avant tout de renforcer les défenses de l'organisme plutôt que de s'en prendre seulement à l'agent pathogène (bactérie, virue, tumeur). Cette théorie rend compte du fait que certaines maladies sont influencées par l'emploi de la cortisone et d'ACTH, parce que ces hormones fournissent précisément l'équilibre principal entre l'agent pathogène et la défense organique.

Une innovation qui a été fort appréciée des congressistes prit la forme d'une séance publique d'économie médicale concernant les problèmes des médecins praticiens. Entre autres questions on discuta de l'opportunité pour l'omnipraticien de faire hospitaliser ses malades privés et indigents dans les services de médecine des hôpitaux urbains et ruraux, et de les y traiter lui-même sous la surveillance du bureau médical de l'institution. Ce sujet, nos lecteurs s'en souviendront, a précisément été traité dans ces mêmes pages éditoriales le mois dernier, et ce de magistrale façon par le Dr W. V. Johnston de Lucknow.

En outre, dans le but de donner aux praticiens de la campagne des moyens plus faciles de diagnostic, il a été suggéré de demander à l'Etat d'accorder, sinon gratuitement du moins à bien meilleurs frais, certains examens de laboratoire courants, tels qu'azotémie, glycémie, formule sanguine, etc, et même les examens radiologiques les plus en demande. A cette fin des centres de diagnostic pourraient être assurés par un personnel compétent dans certains hôpitaux urbains et régionaux.

Vu la rareté de plus en plus grande des médecins dans maintes campagnes et régions éloignées, on a aussi devisé de moyens pratiques d'obvier à une situation qui s'avère

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APPLICATION FOR ACCOMMODATION

CANADIAN MEDICAL ASSOCIATION

Montreal, June 18 to 22, 1951

Mail this Form direct to:
The Montreal Tourist and Convention Bureau Inc.,
Room 923, Dominion Square Bldg.,
1010 St. Catherine St. W., Montreal 2, Que.

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.....

critique. D'abord encourager les étudians d'extraction rurale à retourner pratiquer la médecine générale dans leur région; les y aider de façon matérielle, rendre leur vie plus facile et plus agréable, et leur faciliter l'accès à des hôpitaix que l'on fera plus nombreux, mieux outillés et pourvus de spécialistes compétents; organiser des conférences, des symposiums et des cours postscolaires par le truchement des sociétés médicales; donner à l'enseignement universitaire lui-même un caractère plus objectif, plus clinique et moins ''spécialisé'' pour ainsi dire; permettre aux étudiants de prendre contact avec les médecins ruraux qui leur démontreraient sur place les avantages réels de la pratique lucrative de la médecine générale loin des centres urbains. Enfin, pour mieux desservir les pays de colonisation, où la pénurie de médecins se fait surtout sentir, on conseille à l'Etat d'y placer des praticiens à certains endroits statégiques et de les rémunérer généreusement, ainsi que les garde-malades dont ils pourraient surveiller effectivement le travail.

Voilà un pâle résumé de certaines questions qui ont été débattues au XXième Congrès des Médecins de Langue Française du Canada. Il n'y a donc aucun doute que de telles assises médicales, en mettant à l'étude des questions scientifiques et d'intérêt professionnel de cette importance, contribuent grandement non seulement à l'avancement de la science médicale mais aussi au bien-être de notre population. Ces deux objectifs marchent de pair et ne sauraient être atteints sans le concours éclairé de toutes les bonnes volontés.

Newfoundland Division of C.M.A., 1950

The annual convention of the Newfoundland Division of the Canadian Medical Association was held at St. John's from August 31 to September 2. This was the twenty-fifth meeting of the Newfoundland Medical Association, the first under the auspices of the National body since affiliation took place shortly after Confederation in 1949.

The official opening of the Convention by Mayor H. Mews of St. John's was held at Memorial University on August 31. During the next three days lectures were given at Memorial University, with clinical sessions at the St. John's General Hospital and the Sanatorium. Drug exhibits by pharmaceutical firms were on display at Memorial University.

The four-man C.M.A. delegation which attended the Convention consisted of the following: Dr. Norman H. Gosse, Halifax, N.S., President of the C.M.A.; Dr. A. D. Kelly, of Toronto, Ontario; Dr. A. J. Grace, of London, Ontario; Dr. Gordon A. Copping, of Montreal, P.Q. A fifth guest speaker was Dr. Stanton M. Hardy, Medical Director of Lederle Laboratories Division, American Cyanamid Company, New York.

On the morning of the opening day a clinical staff conference was held at the General Hospital at which cases of unusual clinical interest were presented by members of the resident and visiting staff and discussed by various speakers. In the afternoon Dr. Copping addressed the members on ''Mistakes and Pitfalls in Medical Practice''. This was followed by an address on ''Carcinoma of the Rectum and Sigmoid'' by Dr. N. H. Gosse. On the second day, Drs. Grace and Copping conducted combined medical and surgical rounds at the General Hospital in the morning. At the afternoon session Dr. Grace delivered an illustrated lecture on ''Principles in the Management of Abdominal Hernias'', followed by Dr. Hardy who spoke on ''The Present Status of Antibiotic Therapy''. The clinical session for the final day of the Convention was held at the Sanatorium where a symposium on Tuberculosis was presented under the direction of the superintendent, Dr. R. E. Bennett, with addresses on various aspects of the subject by members of the staff. At Memorial University later in the day, Drs. Grace and Copping spoke respectively on ''The Management of Varicose Veins'' and ''Congestive Heart Failure''.

During the Convention, meetings were held under the chairmanship of Dr. W. J. Higgins to consider plans for setting up a Newfoundland Branch of the Defense Medical Association. This Association is a liaison organization of the Medical Services of the Armed Forces and the medical profession for the dissemination of knowledge of medical matters pertinent to the defense of Canada. The annual business meeting was held at the Newfoundland Hotel, on September 1. Officers of the Association for the coming year were elected as follows: President—Dr. H. D. Roberts, St. John's; First Vice-President—Dr. R. F. Dove, Corner Brook; Second Vice-President—Dr. A. MacNamara, St. John's; Secretary-Treasurer—Dr. C. Pottle, St. John's.

Social events included a reception and dance at the Old Colony Club on August 31, a luncheon at the Newfoundland Hotel with the Hon. J. R. Chalker, Minister of Health as guest speaker on September 1, and a dinner at the close of the Convention on September 2.

Saskatchewan Division

The Annual General Meeting of the Saskatchewan Division was held in Saskatoon at the Bessborough Hotel, September 14, 15 and 16, 1950. Registered attendance was over two hundred and the meetings were well attended. In the business affairs of the profession in the province considerable stimulation was introduced by the general practitioner's section. This resulted in excellent discussion of professional problems and bids fair to further increase the interest in and knowledge of professional affairs among all members.

We were happy to have as our guests both for scientific presentations and non-scientific talks, Dr. Norman Gosse, President of the C.M.A., and Dr. Margaret Gosse, Dr. H. B. Atlee, Halifax, Dr. H. H. Campbell, Toronto and Dr. J. W. Abbiss, Halifax. Dr. Routley was with us again not only for instruction on C.M.A. affairs but that we might receive the benefit of his world trip and to learn of his experiences. We were pleased at this meeting to see the Faculty of Medical Sciences, University of Saskatchewan take its place in medical affairs by putting on a morning of clinical instruction in the new Medical College Building.

Another outstanding feature of the meeting was a luncheon on Saturday, September 16, at which Dr. E. C. McCoy of Vancouver presented an address on behalf of the General Practitioners' Section of the Canadian Medical Association. Great interest was shown in the subject and there have been many requests for copies of Dr. McCoy's remarks.

Annual Meeting of the Manitoba Division Canadian Medical Association

The Annual Meeting of the Manitoba Division of Canadian Medical Association was held in the Royal Alexandra Hotel, Winnipeg, October 3, 4, 5. The morning sessions on October 3 and 5 featured clinical meetings at St. Boniface and Winnipeg General Hospitals respectively. The afternoon and evening sessions of October 4 were devoted to the business of the Division, and the meeting closed with a dinner and dance on the evening of October 5.

The election of officers resulted as follows: Dr. Eyjolfur Johnson, Selkirk, President; Dr. A. M. Goodwin, Winnipeg, first Vice-President; Dr. C. W. Wiebe, Winkler, second Vice-President; Dr. C. B. Schoemperlen, Winnipeg, Honorary Secretary; Dr. Ruvin Lyons, Winnipeg, Honorary Treasurer.

The visiting speakers, Dr. Norman H. Gosse, Halifax, President of the Canadian Medical Association; Dr. H. B. Atlee, Halifax; Dr. J. W. Abbiss, Halifax; and Dr. F. W. Jackson, Ottawa, were warmly welcomed and their addresses received eager attention.

Dr. Gosse emphasized that the Canadian Medical Association must stand united to prevent government control of medicine in Canada. He stated that everything which reduced man's sense of personal responsi-

bility tended to a reduction of his dignity and ultimately to his complete degradation. He praised the pattern of medical care now being worked out in Australia by Sir Earle Page, the new Minister of Health in that Commonwealth, as one which might well become a pattern for all democratic countries. In the eyes of the Medical profession, Dr. Gosse said, health should be administered by an independent non-political representative commission.

In his presidential address, Dr. D. L. Scott, Winnipeg, voiced strong opposition to government control of medical service. He reviewed the steps which had led to the formation of the prepaid medical scheme, Manitoba Medical Service, sponsored by the Manitoba Division, C.M.A. If the members of the Division backed this plan whole-heartedly, Dr. Scott said, it could easily become a framework for Manitoba's part of a prepaid medical care plan for Canada.

Dr. F. W. Jackson, Director of health insurance studies in the federal Department of Health and Welfare, and formerly deputy minister of health for Manitoba, reviewed the progress of the national health grants program. With the knowledge and experience which can be pooled, a plan could be devised, he said, which would ultimately provide the service which all desire and which will be satisfactory to all. ROSS MITCHELL

CORRESPONDENCE

Megaloblastic Anæmia of Pregnancy

To the Editor:

I was most interested in the article by Drs. Goldenberg and Wyatt on Megaloblastic Anæmia of Pregnancy which appeared in your issue of September. Whilst working in Professor L. J. Davis' blood clinic at the Royal Infirmary, Glasgow, I had the opportunity of seeing such cases, and perhaps it would not be out of place to comment on two features of the above mentioned paper.

Increasingly the tendency in modern hæmatological practice is to report hæmoglobin in grams per 100 millilitres and, coupled with red cell count and hæmatocrit reading, to report mean corpuscular volume and mean corpuscular hæmoglobin concentration routinely. In the malady under consideration a "dimorphic" picture in the peripheral blood is by no means rare. In other words, a stained smear shows a variable degree of anisocytosis and macrocytosis coupled with hypochromia. The degree of iron deficiency may not be appreciated if only the colour index is considered, but a low mean corpuscular hæmoglobin concentration will indicate the need for supplementing folic acid with iron. The alternative is to wait until induced or spontaneous remission of the macrocytic anæmia uncovers the lack of iron.

As far as the distinction from true Addisonian pernicious anæmia is concerned, in those cases of megaloblastic anæmia in pregnancy associated with histamine-fast achlorhydria it is of course justified to administer to pregnant women a known potent liver extract as a therapeutic trial. Should no response be forthcoming, as in the case reported by Goldenberg and Wyatt, the folic acid should be employed. At the termination of pregnancy all treatment would be withheld and the case followed by accurate peripheral blood examinations at least monthly during the first year and every two or three months until two years have elapsed.

A somewhat more technical point is that the sternal marrow picture in these cases frequently is of megaloblastic changes somewhat less intense than in Addisonian pernicious anæmia in relapse, and I have seen at least one case in which the megaloblastic change was at first examination doubtful and a definite diagnosis could only be made after a period of observation.

CECIL HARRIS

Group Practice and Medical Education

To the Editor:

I have just read Group Practice and Medical Education, by Dr. Thorlakson. What his group has done for the University of Manitoba is remarkable and one can not discount the individual ability of the members of the clinic. I have heard the statement made that there is not a month passes in which some American publication has not an article on the Mayo Clinic. This I am sure is excellent publicity from a business standpoint and is necessary perhaps to keep such a large corporation sound financially. Of course medical subjects are always good news and it is said that in order of popularity in the press articles on medical subjects are third, only exceeded by sex and crime stories. Dr. Gallie in the Eighth Listerian Oration may have been speaking casually and I am sure would not condone the efforts of many so-called Clinics to corral all that is profitable in medicine where they are located. It would seem that hospitals are so well equipped today for diagnosis and administered by qualified specialist staffs that that is about all that is necessary in the way of clinics. When a group of men, say an internist, surgeon, laryngologist, join together to save expense for office space and in this way can employ a radiologist and laboratory technician one can not be critical, but where an organization is incorporated with a large staff of nurses and technicians and specialists in every branch, and where the charges are based on the study of each patient's financial standing by an expert accountant one wonders whether the business success of the Clinic might not overshadow its medical side. Where a Clinic only accepts referred patients or those who come directly to the Clinic for treatment nothing can be said. Where a Clinic contracts with large corporations, hotels, insurance companies, etc., to do all examinations and treatment for a certain amount it certainly is no help to the practitioners in that community. Group practice is here to stay, but only where it makes for better diagnosis and reduces office expense, not where it interferes with individual practice by both general practitioners and specialists. F. B. BOWMAN

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SPECIAL CORRESPONDENCE

The London Letter

(From our own correspondent)

TOBACCO AND CANCER

A report on "Smoking and carcinoma of the lung" just published in the *British Medical Journal* is in striking agreement with recent reports from the United States. It is based upon an investigation of 709 cases of carcinoma of the lung (649 men and 60 women) in London hospitals. Of the male patients, only 0.3% were non-smokers, whilst 31.7% of the female patients did not smoke. The corresponding incidence of non-smokers in the control group of 709 patients without cancer was 4.2% for men and 53.3% for women. A relatively high proportion of the patients with cancer of the lung were heavy smokers; for instance, 26% of the men and 14.6% of the women smoked 25 cigarettes or more daily, compared with only 13.5% of the males and none of the females in the control group. Cigarette smoking appeared to be more dangerous than pipe-smoking, but inhaling seemed to make little difference. It is concluded that "smoking is an important factor in the cause of carcinoma of the lung".

WHOOPING COUGH PROPHYLAXIS

The Manchester health committee, one of the most progressive public health authorities in the country, has submitted to the city council a plan for the in-

oculation of 20,000 children against whooping cough. The work is to be done in collaboration with the Medical Research Council. The children to be treated will be in the age-groups six months to four years, and each child will be given three injections. A careful follow-up of all inoculated children is to be maintained, and each child will be seen every month for two years. This welcome move in preventive medicine will go far towards bringing this country into line with the more progressive municipalities of Canada and the United States.

Proprietary Medicines

The latest development in the laudable attempt to control the expenditure on drugs under the National Health Service is the publication by the Ministry of Health of a list of some 700 proprietary medicines advertised direct to the public. A copy of this list has been sent to every doctor in the country, accompanied by a letter from the Chief Medical Officer of the Ministry. This letter points out that there has recently been a recommendation that no medical preparation advertised to the public should be prescribed under the National Health Service. After explaining that this list has been prepared so that doctors may be aware of what preparations come into this category, the letter goes on: "I am, therefore, writing to ask you to try to avoid the prescribing under the National Health Service, of any of the substances on this list unless, in your professional judgment, you feel clear that there is some special justification for doing so in any individual case". An interesting legal point which may need to be decided one of these days is the precise definition of what is meant by "advertised direct to the public".

Changing Doctors

One of the many minor irritations of the National Health Service to general practitioners has been the tendency of a certain number of patients to change from one doctor to another at frequent intervals at short notice and for no good reason. Hitherto it has been possible for a patient to change merely by going to another doctor in the same district who was willing to accept him (or her). This excessive liability of choice has also caused considerable administrative inconvenience. In future, unless he has changed his place of residence, no patient will be able to change unless he has either obtained the consent of his present doctor or has sent notice of his desire to transfer to the local executive council. In the latter case the transfer cannot take place until a fortnight after the council has been notified. Should the patient move to a new address, of course, he will be able to transfer to a new doctor immediately. This procedure will involve no hardship in genuine cases, but will go far towards checking the roving propensities of a certain type of patient all too well known to general practitioners all over the world.

William A. R. Thomson

London, October, 1950.

ABSTRACTS FROM CURRENT LITERATURE

Medicine

Late Non-tuberculous Complications of Calcified Hilus Lymph Nodes. Head, J. R. and Moen, C. W., *Am. Rev. Tuberc.*, **60:** 1, 1949.

In most instances, primary tuberculosis of the lungs is a benign infection; the parenchymal and hilar lymph node focus each progressing to spontaneous arrest and calcification. Complications may occur and are due to rupture of the nodes into surrounding tissue, progression to tuberculous pneumonia, involvement of the thoracic dust, and production of atelectasis which may lead to epituberculous pneumonia or chronic non-tuberculous bronchiectasis. Later, a still active node may be a source of reinfection tuberculosis. The present study is concerned not with the tuberculous complications of the acute phase but with the late non-tuberculous activation of the calcareous nodes. This condition is not rare and can cause nearly every type of pulmonary infection.

It is uncertain how healed, calcified and innocuous lymph nodes suddenly become secondarily infected and enlarged to press upon, occlude and perforate the bronchi. The calcium, like any other foreign body, is easily infected and the infection persists until the foreign body is removed. The most likely route by which bacteria could reach calcified nodes is by the lymphatics from infection of lung parenchyma. A narrowed bronchial lumen predisposes to infection in the distal bronchi and parenchyma. The authors confirm, from fifty cadaver dissections, that the most frequent sites of stricture and perforation were in those portions of the bronchi where lymph nodes were normally found. In the present series the frequency of involvement was distributed among the right upper, the left upper, and the middle lobe bronchi, respectively.

The basic pathology of bronchial ulceration, narrowing and occlusion produces a clinical and roentgenographic picture that can simulate any acute and chronic bronchial and pulmonary disease. Complications include bronchopneumonia, bronchiectasis, atelectasis, lung abscess and all types of chronic pulmonary suppuration. Frequently the condition is scarcely distinguishable from bronchial carcinoma.

Activation of lymph nodes is frequently associated with the dramatic expectoration of calcium stones. The patient often fails to be impressed with this finding and he should always be questioned on this specific point. Other clinical features vary with the associated pathology. Blood-streaking or frank hæmorrhage are common and may be the only symptom. There may be merely recurring attacks of pneumonia in the same lobe. The cough associated with this is often severe and spasmodic. During the acute stage a persistent localized wheeze is a common and suggestive sign. Chest pain is often severe in acute atelectasis. Attacks tend to be recurrent and the symptoms usually stop when all the calcium has been extruded.

To diagnose this condition one must remember that hilar calcifications may cause parenchymal disease. Radiological findings are as variable as the pulmonry conditions produced. Bronchoscopy rarely shows more than granulation tissue and bronchial narrowing. Laminography may reveal a node impinging upon a bronchus. Treatment depends upon the nature and extent of the associated pulmonary pathology.

J. F. Simpson

Pulmonary Hypertension in Heart Disease. Borden, C. W., Ebert, R. V., Wilson, R. H. and Wells, H. S.: *New England J. Med.*, **242:** 529, 1950.

The pulmonary circulation is of paramount importance in heart failure and pulmonary hypertension has been a well recognized effect of mitral stenosis for many years, giving rise to the accentuated pulmonic second sound, the Graham-Steell murmur, the dilatation of the pulmonary artery and right ventricle, and right axis deviation in the electrocardiogram. Pulmonary hypertension in left heart failure is only present during attacks of so-called cardiac asthma.

Catheterization of the right side of the heart has confirmed the above. The normal pressure in the pulmonary artery has been found to be about 20 systolic and 9 diastolic. In 31 patients with mitral disease an abnormally high pressure was found which roughly correlated the functional capacity of the heart, the worse the clinical condition the higher the pulmonary hypertension. In 23 men with left ventricular failure all but three showed elevation of pulmonary pressure

but not to the extent of the patients with mitral disease. The pulmonary blood flow in this group was significantly reduced but again this reduction did not equal that of the group with mitral disease. No correlation was found between reduction in vital capacity and the pressure in the pulmonary artery, indicating that reduced vital capacity is related to pulmonary œdema rather than to pressure changes in the pulmonary vascular system. NORMAN S. SKINNER

The Clinical Importance of Coagulase-Positive, Penicillin-Resistant Staphylococcus Aureus. Beigelman, P. M. and Rantz, L. A.: *New England J. Med.*, **242:** 353, 1950.

Fifty-six per cent of 64 strains of coagulase-positive *Staph. aureus* obtained from clinical material by the authors, between August, 1948 and May, 1949, were penicillin-resistant; 20% of these resistant organisms were recovered from patients who had not received penicillin; 35% of strains of *Staph. aureus* isolated from the noses of healthy children were insensitive to penicillin despite the fact that penicillin had not been used in these cases. The frequency of occurrence of penicillin-resistant *Staph. aureus* is increasing in clinical practice. This is due to the previous use of penicillin and also to cross-infection of hospital patients with resistant strains. Probably the best form of therapy in such cases is a combination of aureomycin and streptomycin.

NORMAN S. SKINNER

Pheochromocytoma. Smithwick, R. H., Greer, E. R., Robertson, C. W. and Wilkins, R. W.: *New England J. Med.*, **242:** 252, 1950.

Pheochromocytomas are rare tumours, arising in chromaffin tissue, which may cause hypertension which is usually paroxysmal but may be sustained (in about 25%) and simulate essential hypertension. The most common site of origin is the adrenal medulla, the next most common is the organ of Zuckerkandl just above the aortic bifurcation, but it may occur in chromaffin tissue in the chest or lumbar region. The right adrenal is involved about twice as frequently as the left. Two tumours are present in about 20% of cases.

The authors have studied eleven cases of pheochromocytoma, three of which were diagnosed prior to, and the remainder during the course of, sympathectomy. Symptoms and signs in these cases, and in 107 cases from the literature, were studied in an effort to arrive at a diagnostic pattern which would allow clinical differentiation from essential hypertension.

Excessive sweating and peripheral vasomotor phenomena (coldness of hands and feet, blanching of fingers, mottled bluish-red discoloration of the legs or hands) are very common in cases of pheochromocytoma but are rare with essential hypertension. Elevation of temperature of a degree or more occurred in about 70% of all the tumours. A normal cold-pressor response is the rule in pheochromocytoma and the exception in hypertension. Elevation of the blood sugar and of the basal metabolic rate should make one suspicious of pheochromocytoma, as should postural hypotension and postural tachycardia, as these symptoms occur much more commonly than they do with essential hypertension.

An intravenous pyelogram will occasionally assist in the diagnosis of a pheochromocytoma, provided the tumour is large enough. Perirenal injection of air has confirmed the diagnosis at times but there is a definite danger of air embolus.

The injection of histamine, methacholine chloride and tetraethylammonium bromide may precipitate a paroxysm of hypertension and confirm the diagnosis and while this procedure is probably reasonably safe in cases with a normal pressure at the time of the test, an epinephrine-blocking agent should be at hand if needed to terminate the attack promptly should alarming symptoms result. NORMAN S. SKINNER

Surgery

The Use of Tantalum Gauze in the Repair of Hernias with Tissue Deficiencies. Dunlop, G. B.: *New England J. Med.*, **242:** 542, 1950.

Tantalum gauze provides a satisfactory method of repair for most large inguinal hernias with tissue defects. After five days in hospital, and two or three weeks at home, most patients can safely return to work. It can also be satisfactorily employed in the repair of ventral hernias. An anatomic repair can be carried out utilizing fascial layers sutured without tension, replacing tissue deficiency with the tantalum gauze. In the case of inguinal hernias the spermatic cord may be left in direct contact with the gauze without danger of injury.

The author reports on 61 hernias complicated by tissue defects in which tantalum gauze was used. There were two unilateral recurrences, on difficult bilateral repairs done in early cases, where the cord was transplanted and before it was realized that such transplantation was unnecessary. During the same period 420 inguinal hernias were repaired without the use of tantalum gauze, which is only necessary where a tissue defect is present. NORMAN S. SKINNER

Obstetrics and Gynæcology

Premenstrual Tension. Morton, J. H.: *Am. J. Obst. & Gynec.*, **60:** 343, 1950.

Investigation of 29 women with premenstrual tension indicates that the symptomatology is the result of an estrogen-progesterone imbalance with a *relative* excess of œstrogen, due to deficient progesterone secretion. This conclusion was reached on the basis of endometrial biopsies, vaginal smears, basal temperatures, and urinary hormone assays. The unopposed œstrogen displays its activity by stimulating increased proliferation in the breasts and pelvic organs, by altering electrolyte and water metabolism to allow increased retention of extracellular tissue fluid, and by altering carbohydrate metabolism to permit increased sugar tolerance.

A new and striking finding in premenstrual tension is the hypoglycæmia. This is clinically manifested by increased appetite or a craving for sweets, and a trembling of the hands described by the patients as the "shakes". The psychic manifestations as well as the weakness and fatigue are also largely ascribed to the hypoglycæmia. The anxiety neurosis, when present during the hypoglycæmic state, is probably a subjective reaction to the profound weakness and fatigue.

The treatment of premenstrual tension is directed toward the correction of hormonal imbalance. Symptomatic treatment of the œdema by salt restriction and administered diuretics, and of the hypoglycæmia by dietary measures, are helpful adjunct measures.

ROSS MITCHELL

Coagulation Defects Associated with Premature Separation of the Normally Implanted Placenta. Weiner, A. E., Reid, D. E. and Roby, C. G.: *Am. J. Obst. & Gynec.*, **60:** 379, 1950.

A defect in the coagulation mechanism may develop in premature separation of the placenta. The blood changes are characterized by a decrease in the fibrinogen concentration and prothrombin activity and the presence of a circulating fibrinolysin. These changes have been observed in cases of severe premature separation of the placenta. They are not evident in the mild type of premature separation. The detection of these blood changes requires repeated observations of the size and stability of the clot formed by the patient's venous blood when incubated at 37° C. Replacement therapy with fibrinogen and blood is of primary importance in the treatment of severe premature separation of the placenta. ROSS MITCHELL

Insulin-Induced Skeletal Abnormalities in Developing Chickens. Duraiswami, P. K.: *Brit. M. J.*, **2:** 384, 1950.

Though genetic factors play an important part in the causation of congenital abnormalities, it has been shown in recent years that certain environmental factors can interfere with the normal developmental processes in the embryo. An account of the skeletal abnormalities induced by insulin has been given. It has been suggested that unchecked insulin hypoglycæmia during the early stages of development may adversely affect the development of the cartilaginous skeleton and of the eyes by depriving them of their essential constituent mucoprotein to varying degrees. ROSS MITCHELL

Congenital Atresia of the Œsophagus. Belsely, R. H. R.: *Brit. M. J.*, **2:** 324, 1950.

Congenital atresia of the œsophagus is commoner than is generally realized, the incidence probably being one in 800 births. Cases are missed clinically or at necropsy because they are considered to have developed pneumonia or to have atelectasis. Diagnosis is easy once the condition is suspected. An infant that brings up an undue amount of mucus, particularly as a fine froth, for several hours after birth should be suspected of atresia, and such an infant *should not be fed by mouth until the condition has been excluded.* Diagnosis can easily be confirmed by passing of a medium-sized rubber catheter. Operation holds out good prospects of cure if these cases are diagnosed early and operated upon promptly. Operation is hardly worth attempting unless there is available an anæsthetist with special experience in thoracic surgery, and preferably one who has made a special study of anæsthesia in infancy.

Ten cases treated by operation are recorded, five of whom survived. Continual aspiration of mucus from the mouth and pharynx, both before and after operation, is necessary. The transpleural approach has been used in all five successful cases. Closure of the tracheo-œsophageal fistula and restoration of bowel continuity by the simplest form of one-layer end-to-end anastomosis is the operation of choice. Attention to the blood supply of the lower segment should reduce considerably the risk of a breakdown of the anastomosis and its attendant disasters.

Feeding by mouth can be resumed 24 hours after operation, or earlier, and a gastrostomy appears to be unnecessary in the uncomplicated case. ROSS MITCHELL

Anæsthesia

The Administration of Nitrous Oxide and Oxygen. McCarthy, K. C.: *Anæsthesiology*, **2:** 485, 1950.

The author stresses the many desirable attributes of nitrous oxide as an anæsthetic agent. It is nonirritating, almost imperceptible in odour, and induces loss of consciousness rapidly. Although not a potent agent it produces anæsthesia adequate for extra-abdominal procedure. It causes the least postoperative vomiting and morbidity of any of the anæsthetic agents if the associated oxygen supply is adequate. It is in these respects however that there has been much dissension. Is it possible to produce and maintain adequate anæsthesia with nitrous oxide and at the same time avoid oxygen shortage, or its use commonly associated with so much hypoxia that serious sequels, chiefly neurological, are to be expected?

The author makes a good case for nitrous oxide showing that it is not always accompanied by hypoxia even when given with oxygen in proportions less than that found in atmospheric air at sea level, and points out that in aviation, altitudes of 11,000 to 12,000 feet, supplying as little as 12 to 13% oxygen, are tolerable to average individuals. He stresses the importance of premedication with adequate morphine to reduce the metabolic rate and permit the administration of more nitrous oxide and less oxygen in order to obtain a better anæsthetic effect. He does not favour complete rebreathing technique as it allows accumulation of nitrogen which interferes with the action of nitrous oxide by dilution. He suggests a fractional breathing technique as being more satisfactory. Leaks in the system are disastrous to good nitrous oxide anæsthesia as they allow dilution by the air and an accompanying lack of pressure of the gases inhaled by the patient. F. ARTHUR H. WILKINSON

Pathology

Coexistant Bronchogenic Carcinoma and Active Pulmonary Tuberculosis. Robbins, E. and Silverman, G.: *Cancer*, **2:** 65, 1949.

The nature of the relationship between pulmonary carcinoma and tuberculosis, the idea that the two diseases were antagonistic and the apparent increase in the number of cases of coexistent disease have produced lively speculation for years. The incidence of carcinoma of the lung in cases of tuberculosis is about 1.5%. The incidence of tuberculosis in cases of carcinoma is more difficult to establish and there is considerable variation in the data. The material presented in this study consists of eleven cases of primary bronchogenic carcinoma, all with coexistent active pulmonary tuberculosis. The cases were assembled from the protocols of about 6,900 consecutive autopsies at a general hospital and a sanatorium.

All the cases were in men who ranged from 46 to 62 years, with an average of 54 years. All patients had a productive cough and eight complained of chest pain. In six of these the pain was present on the side of the carcinoma. Only one patient had blood-tinged sputum and none had gross hæmoptysis. All were febrile during some or all of their hospital course. Clubbing of the fingers was present in only two cases. The cases from the sanatorium were all diagnosed as far-advanced bilateral pulmonary tuberculosis, all had positive sputum and the established diagnosis tended to obscure the significance of the signs and symptoms suggestive of neoplasm. In contrast, four of the five cases from the general hospital were diagnosed as carcinoma and had negative sputum. The only case considered to be pulmonary tuberculosis was the one with a positive sputum.

The apparent increase in incidence of coexistent pulmonary tuberculosis and pulmonary carcinoma is due to the fact that individuals with tuberculosis are today entering an older age group. The general and local effect of carcinoma favour the progress of tuberculosis but there is no evidence to prove that it predisposes to tuberculous infection. Conversely, it can not be shown that pulmonary tuberculosis favours the development of carcinoma. Therapeutic irradiation carries a hazard of activation of a coexistent tuberculosis. Severe or prolonged chest pain in a patient with tuberculosis warrants investigation for a coexistent carcinoma and multiple sputum examinations should be done in cases of carcinoma of the lung with bilateral infiltrations.

J. F. SIMPSON

Psychiatry

Further Experiences of the Use of Malononitrile in the Treatment of Mental Illnesses. Hartelius, H.: *Am. J. Psychiat.*, **107:** 95, 1950.

This is the latest report in English from the Swedish Clinic where this treatment was developed. It includes a criticism of the paper by MacKinnon, Hoch, Cammer and Waelsch previously abstracted in this Journal. The author attributes the negative results of these workers to an insufficient duration of each treatment and possibly an impure form of the drug under trial. He reports 40 recent cases in addition to ones previously treated. The patients were given 2.4 mgm./kg. body weight of malononitrile, allowed to act for about 48 minutes, and then counteracted by 15 ml. of 5% sodium thiosulphate. The average number of treatments was 8, given twice a week. Endogenous depressions were in the majority of the patients treated and showed the best results. Although admitting that controls were lacking and the number of cases inadequate statistically, the

author compared the favourable results, described as "mental stimulation", with the results of electro-convulsive therapy. He considered that they were of the same order, with the advantage of less risk and of lack of the contraindications which prohibited E.C.T. in several of the patients, such as cardiac conditions, and intellectual occupations which might be prejudiced by the temporary memory impairment of E.C.T. W. DONALD ROSS

Medical Education for Insight. Evans, L. J.: *Am. J. Orthopsych.*, **19:** 585, 1949.

According to this administrator of foundation funds, medical practice is at a crossroad at which there are deficiencies in the preparation of doctors for their most effective service to their patients and greatest satisfaction to themselves. In spite of increased specialization and devices such as group practice, the heart of medicine is still the relationship between the doctor and a person who comes to him for help. The present curricula in most medical schools fall short in giving the medical student an understanding into that relationship. Dr. Evans proposes the devotion of more time during the first two years of the medical course to the study of normal human growth and development, including the importance of interpersonal relationships. Such a program would involve more teaching early in medical school from social workers, psychiatrists, public health physicians, and nurses. The author predicts the improvements in insight about his own rôle which would accrue to the physician in training and suggests more ideal patterns for physicians of the future in one of several rôles, according to his predilections: as a general physician, as a clinical specialist, as a public health, hospital, or community medical care administrator, or as a teacher and investigator. W. DONALD ROSS

Industrial Medicine

Fluoroacetate Poisoning . . . a Review and Report of a Case. Gajdusek, D. C. and Luther, G.: *Am. J. Dis. Child.*, **79:** 310, 1950.

Since the war, sodium fluoracetate, commonly called "1080" has obtained widespread use as a potent rodenticide. In addition, due to its varied pharmacologic properties it has become increasingly important in laboratory studies. Experimental study during and since the war has indicated that sodium fluoroacetate is one of the most poisonous substances known. A search for an antidote has been made. In this article the authors report a case of human poisoning by this substance—the first such case ever reported. The patient was a two year old Nego boy who licked the top of a bottle of rat poison. The exact dose is unknown but investigation revealed that the child undoubtedly obtained relatively pure sodium fluoroacetate. As in experimental animals, cardiac and central nervous system symptoms predominated, but the child made complete recovery without sequelæ. One year after his discharge from hospital he appeared normal and healthy.

From observations in this case and in the experimental work with animals, the authors have drawn certain conclusions: In human poisoning with fluoroacetate, cardiac and central nervous system effects are both important, the central nervous system effects predominating. The clinical picture closely parallels those seen in experimental poisoning in laboratory animals. No antidote is available but sedation with barbiturates offers a possible means of combating the convulsions. Because of danger of respiratory depression and cessation, a respirator should be kept on hand and artificial respiration started immediately if prolonged apnœa appears. It is not certain in the case reported whether the calcium therapy given early, really influenced the outcome. The immediate improvement noticed with its administration, however, would warrant its use again in future cases. Experimental experience with monkeys as reported earlier in the literature indicates the intracardiac use of procaine hydrochloride and cardiac massage if ventricular fibrillation should occur.

In a footnote the authors refer to another case of this poisoning in a child, referred to in literature subsequent to the completion of their report. In this instance the child's convulsions were controlled by pentobarbital sodium; ethanol also was given. This child too, survived. The investigators who reported this, also reported decreased mortality due to fluoroacetate poisoning in animals treated with 10% solution of ethanol in isotonic sodium chloride solution given subcutaneously within ten minutes of injection of the poison. Its value in human cases is unknown.

MARGARET H. WILTON

OBITUARIES

Dr. William Webb Alexander, one of the oldest graduates of McGill University, died in Montreal, September 20, after a lengthy illness. He was in his 85th year. Born in Charlottetown, Dr. Alexander studied at Prince of Wales College there before entering McGill University from which he graduated in medicine in 1891. After interning at the Montreal General Hospital, Dr. Alexander practised at Hemmingford, Que., for several years, and in 1895 moved to Lachute, Que., where he practised until 1918. He was a member of the Medico-Chirurgical Society and of Isaac Henry Stearns Masonic Lodge. Survivors include his widow, a son and a daughter.

Dr. John Fettes Anderson died in Port Alberni on August 20. Dr. Anderson was born in Vancouver in 1923. After graduating from Prince of Wales High School, he took his pre-medical course at University of B.C. and graduated in medicine at University of Manitoba. He interned at Vancouver General Hospital and practised at Campbell River and Alberni for two years. He was well known in fishing and sports circles on Vancouver Island, and took great interest in Indian affairs. Dr. Anderson is survived by his wife and an infant daughter.

Dr. Joseph Honore Authier, recently elected Mayor of Ville St. Laurent, died on August 27. He was in his 53rd year. Mayor Authier was a member of the local Medical Society and attached to the Association des Médecins du Nord. He graduated with a medical degree from the University of Montreal in 1920. One of the founders of de l'Esperance Hospital, Mayor Authier spent much of his time in contributing to the progress and development of the establishment. He is survived by his widow and a daughter.

Dr. J. R. Beaven died at Parry Sound Hospital on September 15. Dr. Beaven, who was in his 62nd year, was born in Hespeler. He was educated at the Hespeler public school and the Galt Collegiate and graduated from University of Toronto Medical School with high honours. In the First Great War he joined the Harvard University Medical Unit and had four years' service overseas. At the end of the war he came to Galt and opened a practice. Over the years Dr. Beaven developed a large practice and became widely known as one of the leading surgeons of this district. Following his illness he limited his practice to the care of his old patients. "Reg" Beaven, as he was known to his close friends, was a keen sportsman, a supporter in all its branches, and was especially interested in rugby, a game in which he took part when attending the collegiate. He was a backer of local rugby clubs. He was a member of the Galt Curling Club and the Waterloo Golf and Country Club and was widely known among devotees of these games throughout the province. For a number of years he took part in the annual bonspiel at the Seignory Club in Quebec. He was also an ardent fisherman, a member of the Seminole Club. Dr. Beaven is survived by his widow, one daughter and one son.

Dr. Morley E. Branscombe who died at Picton on September 18, was born in Prince Edward County and received his early education at the public school, high school and Albert College. Later he entered Queen's University, Kingston, and after receiving the degree of B.A., he commenced the study of medicine and graduated with the degree of M.D. in 1904. Following graduation Dr. Branscombe interned at the Ottawa General Hospital. Eventually he commenced the practice of his profession in Picton and continued until the First Great War when he enlisted and went overseas. Returning to Canada Dr. Branscombe took up residence in Belleville and engaged in practice until his late illness developed. He was a member of the Masonic Order and a Shriner. Surviving him is his widow.

Dr. Michael James Carney died at Halifax on August 15, 1950, following a long and painful illness. Born in Halifax of an old and prominent family, he was graduated in Arts from Dalhousie University in 1904, and from McGill in Medicine in 1909. After doing special work in pædiatrics he returned to Halifax where he quickly established himself in his specialty. During World War I he served at Cogswell Street Military Hospital, Halifax, and at McNab's Island. Following the war his increasing interest in internal medicine won him an appointment on the medical staff of the Victoria General Hospital, where he was successively Associate and Attending Physician. He was for many years Professor of Pædiatrics at Dalhousie University. Dr. Carney was known in Halifax and far beyond it as the "Doctor's Doctor". His exceptional skill and outstanding diagnostic ability won and maintained their confidence. As a teacher he had the ability, given to few, of lucid explanation of difficult problems. He was one of the most kindhearted men, and his charitable work often seriously encroached on his more remunerative work. He never refused a call; he never denied his best.

Dr. Francis Regis Donnelly, aged 41, died suddenly on August 20 at Massey, Ont. Born at Stanleyville, Ont., Dr. Donnelly received his early education at Perth schools and attended Queen's University, Kingston, where he graduated in medicine. He served as an intern at the Hotel Dieu in the latter city and then took a postgraduate course in New York. Dr. Donnelly practised at Chesterville and Tweed. He also served with the Royal Canadian Army Medical Corps at Owen Sound and Ottawa during the early war years before joining the Sudbury Clinic in 1942, where he spent a year before starting his practice in Massey. Dr. Donnelly was a well-known figure in Massey sporting circles. He was president of the Massey Badminton Club which he formed last fall. He is survived by his widow and two sons.

Dr. Thomas H. Field, aged 59, died in Edmonton on September 11. A specialist in surgery, Dr. Field was a Fellow of the Royal College of Surgeons of Canada and an executive member of the College of Physicians and Surgeons, serving council member from 1941 to 1949 and as president in 1945. He began his practice in Edmonton in 1925 after graduating from McGill University in 1922. A leader in medical and public health work, he was Alberta representative on the Medical Council of Canada from 1944 to 1950. He served on the boards of the Royal Alexandra Hospital and the Alberta Blue Cross. He was also a member of the Alberta Medical Association and the provincial cancer clinic.

Dr. J. Ellis Griffith died on September 6 at his Victoria home. He was 74. Born in Pwllheli, Wales, Dr. Griffith practised in London, England for 18 years before coming to Canada in 1913. He continued his practice in Vancouver until 1946, when he retired and came to this city. He served with the Canadian Medical Corps in the Great War, and was a prominent member of the Cambrian Society in Vancouver for many years. He is survived by two daughters.

Dr. Frank R. Harvey died in Kitchener on August 28. He had been a physician there since 1920. Born at Arthur, he served with the Canadian Army Medical Corps in World War I. He was a graduate of the University of Toronto.

Dr. Brougham F. Johnson died in Saint John on September 29, 1950. Dr. Johnson was 71 years of age. He was a graduate of McGill, 1906, and had practised in New Brunswick until his retirement a few years ago.

Dr. Archibald Duncan McArthur, general practitioner and surgeon in Toronto for many years, died on September 20 at Toronto General Hospital. Dr. McArthur was born at Greenbank. Following graduation in medicine from the University of Toronto, he practised for some years in Blackstock. He was a Fellow of the Royal College of Surgeons and a member of the Masonic Order. He leaves his widow, a daughter and a son.

Dr. Laurel Cole Palmer, aged 63, died on August 24 in Toronto. Dr. Palmer was born in Petrolia. He attended Parkdale Collegiate and graduated in medicine from the University of Toronto in 1914. He was a star football player at university. Early in the First World War he enlisted with the Canadian Ambulance Corps. Serving for five years overseas with the Canadian Army Medical Corps, he held the rank of lieutenant-colonel. Dr. Palmer was for a time chief Canadian surgeon at Moore Barracks in the south of England. He was twice decorated for gallantry in France. While at the front Sir Frederick Banting was one of Dr. Palmer's junior officers. It was Dr. Palmer who recommended Sir Frederick for the Military Cross. He leaves his widow, a son, and a daughter.

Dr. Wilfrid Parent, aged 51, died suddenly on September 4 in Edmundston. He was born in Hamilton and was a graduate of St. Mary's College, Van Buren. He attended the University of Maine one year and was a graduate of Bowdoin College and Jefferson Medical College at Philadelphia, Pa. He served as chairman of the board of selectmen of Van Buren for several years and also served several years with the health and welfare department. He was a fourth degree member of the Madawaska council of Knights of Columbus. Dr. Parent devoted much of his time to civic and community affairs, and will be greatly missed along the St. John Valley. He is survived by his widow, two daughters, and three sons.

Dr. Melville A. Platt, aged 55, died on September 6 at Victoria Hospital, London, Ont. A native Londoner, Dr. Platt graduated from Central Collegiate and entered the University of Western Ontario Medical School in the fall of 1915. He was physician for many years to employees of General Steel Wares. He resided at 360 Queen's Avenue. He is survived by his widow, and two sons.

Dr. George W. Pringle, aged 73, died on September 1 at his summer home at Lake Simcoe. Born at Madoc, Dr. Pringle attended Normal School and was a graduate of Queen's University in both arts and medicine. For some years he was a teacher on the staff of public schools in Saskatchewan and Ontario and was a former principal at Burk's Falls. He established a practice in the Davisville district in 1912. Dr. Pringle had been an examining physician with the London Life Insurance Co. and the T.T.C. He leaves his widow and two daughters.

Dr. Byron C. Reynolds died on September 14 in a Montreal hospital. He was in his 65th year. Dr. Reynolds, a graduate of Queen's University of the class of 1909, had served overseas as a captain in the Royal Canadian Army Medical Corps in Salonika, Greece, and later practised in Ottawa. He was for many years a member of the Ottawa Kiwanis Club.

Born in Prince Edward Island he received his early education in Lansdowne, Ont., and Athens, Ont.

Lieut.-Col. O. W. Stewart, formerly chief neurosurgeon of the Canadian Army, died in Montreal on September 22, in his 44th year. Born at Muskogee, Okla., Dr. Stewart graduated from the Oklahoma Medical School, and spent four years at the Massachusetts General and Johns Hopkins Hospital in internal medicine. In 1938, he was appointed to the Montreal Neurological Institute, where he served for two years, before enlisting in the No. 1 Neurological Unit at the outbreak of World War II. In England, he was loaned by the Canadian Army to Queen Elizabeth Hospital at Birmingham as neuro-surgeon returning later to Basingstoke as the Army's chief neuro-surgeon. Dr. Stewart was a member of the British Neurological Society and the American Academy of Neuro-Surgery. His widow survives.

Dr. Bruce Cunningham Sutherland, aged 65, died in Hamilton on August 25. Born in Carleton Place, Dr. Sutherland had lived and practised in Hamilton for 31 years. He took his medical course at Queen's University, graduating in 1906. Later he took postgraduate courses in New York City. For a time he practiced in Guelph and Edmonton before enlisting with the Medical Corps and serving overseas. He leaves his widow and one daughter.

Dr. Alexander James Swan who died at his home in Winnipeg on September 27, aged 69. It might be said of him that he had two vocations, medicine and music and that in each he was successful. Born at Greenock, Scotland, he came to Canada in 1903 and seven years later graduated from Manitoba Medical College. His practice at Binscarth was interrupted by the First World War in which he served as M.O. with the Cameron Highlanders of Winnipeg, No. 3 Canadian Casualty Clearing Station and No. 1 Canadian General Hospital. On returning to Canada he practised at MacGregor until 1925 when he moved to Winnipeg. After postgraduate work in London, Vienna and Philadelphia he resumed practice, specializing in eye, ear, nose and throat. On the outbreak of the Second World War he re-enlisted with the rank of Major, R.C.A.M.C. and from 1944 to 1946 he was on the staff of Deer Lodge Military Hospital. He was a lecturer in the Medical Faculty of Manitoba University. In 1933 he was secretary of the medical committee headed by Dr. E. S. Moorhead which was set up by the Winnipeg Medical Society to deal with the problem of providing medical care to indigents. On his retirement from this position he and Dr. Moorhead were honoured at a dinner in the Fort Garry Hotel on April 27, 1934, given by their medical confrères.

Before coming to Canada he had been organist of a Greenock church. As a medical student his musical ability was much in demand and he served as organist at St. Paul's, Westminster and Crescent Churches, later as organist and choir master of First Presbyterian Church, Winnipeg. His wife predeceased him, but he leaves two brothers, Dr. R. R. Swan and Rev. J. A. Swan, two sisters, a son and two daughters.

Dr. Frederick A. Thibeault, a pathologist connected with Toronto Western Hospital for about 30 years, died suddenly in North Bay on September 22. Dr. Thibeault, living in retirement for 20 years, had not suffered any illness. Death came suddenly from a heart attack. He was unmarried and is survived by one brother and four sisters.

Dr. Franz Volhard

AN APPRECIATION

On May 24, of this year Franz Volhard, the dean of German Internal Medicine, died at the age of 78 in Frankfort where he was still fully active as Professor of Medicine and Chief of the University Clinic. Volhard was world famous on account of his classical work on renal diseases. However, he was actually quite encyclopædic in his approach, and his earlier work includes papers on the most diverse topics, such as the discovery of a lipase in gastric secretion, and on the registration of venous pulsation. As a teacher in internal medicine he was extraordinarily stimulating and thought-provoking. His personality had a decisive influence on all those who came in contact with him as undergraduate or postgraduate students. In his teaching he transmitted a great deal of the shrewdly computing methods of pure observation (without laboratory aids) which had been the tradition of the great clinicians of the nineteenth century. For example, he insisted that students must be able to diagnose any type of valvular lesion of the heart purely on the basis of tactile and visual observations, and that auscultation was to be regarded only as a means to confirm the diagnosis.

He upheld a broadly humanist tradition in Medicine, and when the Nazis were in power he was so outspoken in his opinions that he was deposed as Professor of Medicine. The Allied Military Government reinstated him. In spite of his age he still appeared to be in full possession of his creative talent, and he died as the victim of a car accident.

During his life he received many honours from numerous teaching centres in Europe and in North and South America. With his death one of the most representative and colourful figures of European Medicine has disappeared.

KARL STERN

Dr. Philip Weatherbe died at his home in Halifax on September 14. Dr. Weatherbe was born in 1875. After receiving his high school education at Horton Academy he attended Edinburgh University, graduating with a medical degree from that University in 1901. In 1907 he returned to Halifax to begin practice, and in 1910 was appointed a staff surgeon at the Halifax Children's Hospital, which position he retained until his death. He served in the South African war at the turn of the century and during the First World War was a major in the Canadian Army Medical Corps, here serving on the staffs of the old Cogswell Street and Rockhead Military Hospitals. At the close of hostilities he was appointed chief of staff at the Pine Hill Veterans Convalescent Hospital. Dr. Weatherbe was a member of the Halifax Medical Society, the Nova Scotia Medical Society and the Canadian Medical Association. Besides his widow, he is survived by two daughters.

Dr. John West died in Magog on September 1 in his 87th year. Born in Yorkshire, England, Dr. West came to Canada in 1893, and obtained his degrees of M.D., C.M., from McGill University in 1893. He practised for many years in Magog, and was prominent in Masonic circles and in community life here. He leaves his widow.

NEWS ITEMS

Alberta

The Medical Inter North-South golf game was played at Red Deer in early September. Many men enjoyed the fine hospitality of the Red Deer fraternity. The cup was won by Dr. H. E. Duggan of Edmonton. This annual event has become one of the brighter aspects of the good fellowship so readily seen among the profession of this province.

Dr. J. J. Ower former Dean of the Faculty of Medicine of the University represented Alberta at the opening of the new Medical School in Vancouver. We were pleased to have a short visit from Dr. J. B. Collip recently who represented Western Ontario Medical School. Dr. Collip is a graduate of the University of Alberta.

Dr. Colin S. Dafoe, has commenced practice in thoracic surgery in Edmonton. He is a graduate of Queen's University and following postgraduate work in England prior to the war served in the British Army Medical Corps for six years in Africa and Yugoslavia. Following the war Dr. Dafoe took his training in thoracic surgery in England and Stockholm; he holds the degree of F.R.C.S.

Dr. Edgar M. Gee, following his postgraduate work in internal medicine in Montreal and New York has taken up practice in Vulcan. During the war Dr. Gee served with the R.C.N.V.R.

The Institute of Public Health is near completion on the University of Alberta Hospital grounds. It fills a much needed place in the health set-up of the province.

W. CARLETON WHITESIDE

British Columbia

Dr. E. S. Sarvis of Huntingdon, B.C. and Sumas, Wash., has moved to Bellingham, Wash., after twenty-three years in the former location. He will be associated there with Dr. S. R. Boyton, Jr., who is taking a postgraduate course in surgery in the Vancouver General Hospital.

The most important event of the past month, and indeed one of great importance as regards Canadian medicine generally, was the formal opening of the Medical Faculty of the University of British Columbia, on September 6, 1950. The actual work of the first year is now in full swing.

The University is taking its new Faculty very seriously. The laboratories for the study of anatomy, physiology, and so on, are splendidly equipped, and though a good deal of use has to be made of temporary buildings, pending the erection of permanent ones, the actual working machinery is fully up to requirements. The dissecting rooms, for example, with their complete absence of any visible signs of cadavers, all covered by the most up to date monel metal lids—and the corresponding absence of the old familiar effluvium of partially arrested decay, are particularly striking in this regard.

As with all medical schools, the number of men and women accepted is only a fraction of the number who applied. Fifty-seven men and three women form the first year class.

The annual meeting of the British Columbia Medical Association is just over. It has been, one may easily say, one of the most significant meetings this organization has ever held. To begin with, the attendance was very large, twice that of the preceding year. Then this year of Our Lord happens to be the fiftieth anniversary of the founding of the B.C. Medical Association. To celebrate this event a special Golden Jubilee Booklet was prepared, which gave a good many of the historical highlights of the medical history of the past half-century.

The actual meeting was preceded by two others, both held on September 25. The first was the annual meeting of the College of Physicians and Surgeons of British Columbia. This occupied the morning and afternoon, and was marked by some very keen discussion, especially on the matter of Economics. The second meeting, that of the British Columbia Medical Association, was held in the evening, and continued till the small hours. A reorganization of the Association is underway, and there was so much interest taken in this matter that it was impossible to conclude. It was decided, therefore, to call a special meeting of the Canadian Medical Association, British Columbia, as it is now called, within 90 days, to bring the proposals forward, and finally dispose of them.

The actual lectures, clinics, etc. of the meeting, occupied the next three days, and were of the very best. They were well attended, and much appreciated.

We had three visitors, all of whom left a deep impression behind. The first was our President—Dr. Norman Gosse of Halifax. Those who heard his talk at the luncheon of the Division will not soon forget it. His earnestness and sincerity were as obvious as was the long view he takes of the duties and responsibilities of medicine in Canada—and his unswerving devotion to freedom of action for the profession—and his commensurate hostility to regimentation in any form. It is encouraging and cheering to hear such men, and we believe there are very many who think as he does. He took part, too, in the lectures, and his talk on cancer, and the part that medical men must play in the campaign against it, was excellent.

The next of our visitors was that faithful old friend of ours, Dr. T. C. Routley, our General Secretary, who came to us in the course of his world travels. Dr. Routley must sometimes be tired of hearing nice things said about him, and though it is a temptation, we will avoid saying how we welcome seeing him and hearing him speak. In some way all his own, he always manages to have something quite new to say, in a way that makes you think he kept it specially for you. But his value to the medical profession is nowhere better shown than in the fact that always, at any meeting, sooner or later, as the discussion waxes hotter, there is a request for Dr. Routley to tell us what he thinks—and he never fails us.

The third of our visitors to whom we should like to refer is Dr. Victor Johnston, of Lucknow, who came out here, to attend the meeting of the General Practitioners' Section of the Canadian Medical Association (B.C. Section). He certainly made it a thing of supreme importance to the numbers of men who attended these meetings, and again and again they called on him to give them the information and advice that we need so badly. His work in Ontario, and his own breadth of vision and hard common-sense, have made him the outstanding figure in this area of medical politics.

The new President of the British Columbia Medical Association is Dr. S. A. Wallace of Kamloops, who succeeds Dr. J. C. Thomas. Dr. H. A. L. Mooney of Courtenay is President-Elect, while Dr. J. A. Ganshorn of Vancouver will be Vice-President, and Dr. J. A. Turnbull, likewise of Vancouver will be Honorary Secretary-Treasurer.

At the Annual Meeting of the College of Physicians and Surgeons of British Columbia, held on September 23, formal authority was given to the Council of the College to proceed with the erection of the new Academy of Medicine. A full explanation of the financial aspects of the project was given, and the motion passed with no dissentients.

The Annual Report of the Columbia Coast Mission, in its report on the work of the medical side of the Mission, has some very interesting things to say. It operates four small ships, of which one, the *Columbia*, acts as a hospital ship. In the past year, it covered 14,382 miles up and down the coast. Of this distance, 1,507 miles were travelled on emergency calls to sick or injured people. The balance represents its usual rounds on hospital matters, regular clinics, etc. The Mission maintains a fully equipped hospital, (St. Mary's) at Garden Bay, and aged folks' rest houses at Pender Harbour. The land has been cleared during 1949 at Whaletown, Cortez Island, for the John Antle Memorial Clinic. This will begin operating shortly. In all some 10,000 whites and Indians receive service from the Columbia Coast Mission, in its various activities along the Coast north and west of Vancouver.

At a special congregation held on September 27 at the University of British Columbia, ceremonies were held marking the opening of the new Faculty of Medicine. Honorary degrees of Doctor of Science were conferred on the following distinguished medical men, who

are in Vancouver attending the Jubilee Anniversary Meeting of the British Columbia Medical Association: Dr. Detlev Bronk, president of Johns Hopkins University; Dr. James Bertram Collip, Dean of the Faculty of Medicine of the University of Western Ontario, and director of the medical research division of Canada's National Research Council; and Dr. Ray Fletcher Farquharson, professor of Medicine at the University of Toronto, and President of the Canadian Royal College of Physicians and Surgeons.

The recent death of Dr. John Harold White of Vancouver marks the passing of a man who had most to do with inaugurating the School Medical Health Services which are now so prominent a part of the School system of that city today. At the time when he was appointed to the post of director of school medical services in 1923, Vancouver had practically no proper school medical inspection, and Dr. White had to start practically from scratch. He made an outstanding success of the job, and gradually developed a system of school medical officers and nurses which has grown steadily into a complete organization. When the Metropolitan Health Board, covering several adjacent towns and municipalities, was inaugurated in 1936, Dr. White became Director of school health services for the entire area. Unfortunately, ill-health forced him to retire in 1945, but his work remains as a memorial to him.

The City of Victoria, through its City Health Department, is undertaking a health survey of Victoria, and the adjacent municipalities of Saanich, Esquimalt and Oak Bay, as well as the area served by the South Vancouver Island Health Unit. This is in line with surveys being made elsewhere in Canada, and takes the form of a sampling survey. It will, in the words of Dr. J. L. Gayton, medical health officer for Victoria and Esquimalt "Give Canada information on types of sickness, duration, incidence of sickness, causes of sickness, based on various factors such as age, occupation, living conditions, etc., loss of productivity due to sickness and the cost of sickness, and so on". Local health nurses will be employed in the making of visits to homes, gathering information, and will report their findings. The scheme is meeting with a good deal of local favour, and will get off to a full start on October 1, 1950.

J. H. MACDERMOT

Manitoba

Dr. J. C. Graham, Man. '50, has been appointed municipal doctor of Minnedosa during the absence on active service of Dr. H. C. Stevenson.

Recent negotiations between the Canadian Red Cross Society and the Brandon General Hospital have resulted in a free blood transfusion service being available for the hospital.

Manitoba hospitals participating in the Red Cross free blood transfusion scheme include those in Greater Winnipeg, Selkirk, Neepawa, Portage la Prairie, Roblin, Souris, Virden, Steinbach, The Pas and Deloraine. It is hoped to bring Port Arthur, Fort William and other northwestern Ontario towns into the transfusion plan.

The official opening of the Brandon Kiwanis Club's Children's Hospital was held on September 23. The building was formerly known as the isolation hospital and is located near the General Hospital.

Dr. J. N. Andrew, a pioneer doctor of Minnedosa, aged 82, was recently the guest of honour at a dinner given by the Minnedosa Junior Chamber of Commerce.

Hospital tag days were held in Manitou, October 6 and 7, in aid of the new hospital which will be opened in Manitou in December.

On October 4, a meeting of the Manitoba Chapter of the Multiple Sclerosis Society of Canada was addressed by Dr. Leonard T. Kurland of Johns Hopkins University, Baltimore. Dr. J. B. Rollitt, assistant to the President of Manitoba University, presided and Dr. A. T. Mathers introduced the speaker. The topic of Dr. Kurland's address was the incidence of the disease in this area. A careful investigation of cases of this disease will be made.

Dr. P. V. G. Kolka of Blonduous, Iceland, was a visitor to the annual meeting of the Manitoba division of the Canadian Medical Association. He is touring the country at the invitation of the Icelandic National League of America and will represent Iceland at the World Medical Association convention at New York.

Dr. Bernard Zeavin, Winnipeg, a 1950 graduate and winner of the Chown gold medal, has left for Boston to continue postgraduate studies at Harvard University.

ROSS MITCHELL

New Brunswick

Dr. H. Bruce Parlee of Saint John has been appointed district medical officer for the C.P.R. in the New Brunswick Division. Dr. Charles P. Fenwick, Chief Medical Officer for the C.P.R. made the announcement at the same time as he made public the resignation of Dr. D. C. Malcolm, from the above named appointment.

The executive committee of the N.B. Medical Society at their fall meeting in Saint John, September 29, dealt with a long agenda of business, referred from the annual meeting. Discussion of Blue Cross and Blue Shield and a brief on Cancer treatment in the province led to approval of a plan of action.

A. STANLEY KIRKLAND

Newfoundland

While in Newfoundland to attend the annual convention of the Newfoundland Division of the Canadian Medical Association, Dr. A. D. Kelly and Dr. D. Cameron, Deputy Minister of the Department of National Health and Welfare, made a plane and boat trip to some of the remoter medical practices on the south coast of Newfoundland.

Dr. J. B. Squire of the Staff of the St. John's Sanatorium has resigned his position and is taking a two-year course in Radiology at the Toronto General Hospital.

Dr. D. J. Hurley of the St. John's Sanatorium staff will be taking a postgraduate course in Radiology in England.

Dr. D. Cant of Stephenville Cottage Hospital is presently taking a year's leave of absence to do postgraduate work in chest surgery at Mountain Sanatorium, Hamilton, Ontario.

Dr. R. H. Butler, who recently established practice at Musgravetown, is presently on leave to be married. Congratulations are extended.

The medical profession was deeply shocked recently at the sudden passing of Dr. Donald O'Keefe of Western Bay. Sympathy is extended to his widow and family.

CHAS. A. ROBERTS

Ontario

A Tonometer Testing Station has been established at the University of Toronto as a service to the ophthalmologists in this country, with funds provided by the Federal Government under a grant for the Prevention of Blindness from Glaucoma. Oculists, who know or

suspect that the readings of their tonometers are faulty, are invited to make use of this station. The instrument should be forwarded to the Tonometer Testing Station, Room 82, Banting Institute, Toronto.

An eye bacteriology laboratory has been started at the Banting Institute in the Department of Ophthalmology, University of Toronto. The laboratory is under the direction of Dr. H. L. Ormsby assisted by Dr. G. G. Cousineau who has been appointed a Hermant Fellow. The laboratory will serve in close liaison with the Departments of Ophthalmology and Bacteriology. Ophthalmologists may refer their private cases to the laboratory for bacteriological investigation.

The Ontario Federation for the Cerebral Palsied, an organization made up mostly of parents of crippled children, recently held a conference at London. They met with doctors, nurses, teachers and social workers interested in the affliction. The parents are trying to form parent councils for the cerebral palsied in major Ontario centres. They believe that parents must be trained to train their children. Speakers at the conference were Dr. Thomas Coffey, medical director of Woodenden cerebral palsy training centre; Harvey Maurer, principal of Wellesley Public School where Toronto's crippled children are taught; Phyllis Carleton, director of the Red Cross Curative Workshop in Windsor; Dr. Roger Knipe, M.O.H. of the Elgin-St. Thomas health unit; and R. W. Hopper, executive director of the Ontario Society for Crippled Children.

Dr. Ray Farquharson, Professor of Medicine, University of Toronto and Dr. James B. Collip, Dean of Medicine, University of Western Ontario, were granted honorary degrees of Doctor of Science at the opening of the University of British Columbia Medical School at Vancouver.

Dr. Hamnet A. Dixon has been appointed associate professor of dermatology at the University of Toronto.

Essex County Medical Society was addressed in September by Dr. Robert Rider on Vaso-Spastic Diseases; by Dr. A. P. Wilson on the More Common Skin Diseases; by Dr. Wilbert P. Brien on Congenital Polycystic Kidneys with case presentations. The district meeting was held in Windsor on October 3 and 4. At this meeting Dr. Alan Taylor spoke on Normal Ovarian Variants; Dr. T. A. Coffey, Department of Medicine, University of Western Ontario spoke on Physical Medicine in General Practice; Dr. Hugh McAlpine spoke on the Present Status of ACTH and Cortisone; Dr. Fred Johnston of Hamilton spoke on Obstetrics on the March; Dr. George E. White spoke on Newborn Care; Professor A. D. McLachlan spoke on Common Surgical Lesions in Childhood; Dr. Miln Harvey was the dinner speaker.

The ladies were entertained at lunch at Dearborn Inn, Michigan followed by a tour of Greenfield Village.

The National Sanitarium Association has given a free chest x-ray to one million persons. The one millionth person who was x-rayed received a cheque for one hundred dollars from the Association.

District No. 9 met at Sault Ste. Marie on September 10, 11 and 12. Dr. Walter Scriver, Montreal spoke on Diabetes and on Acute Renal Failure; Dr. Wallace Graham, Toronto spoke on Arthritis; Dr. Philip Thorek, Chicago spoke on Intestinal Obstruction.

District No. 11 comprising the metropolitan area of the city of Toronto met on September 12. Owing to bad weather Dr. Miln Harvey and Dr. H. S. Dunham were held up at the Sault but Dr. Fiddes filled in very capably. Reports of the growth, slow but steady, of Physicians' Services Incorporated were given by Dr. M. C. Watson. The need for good public relations was stressed by Dr. A. Kelly and by Dr. William Magner.

Dr. P. R. Cannon, professor of pathology, University of Chicago was the speaker at the fifth annual MacGregor Memorial Lecture, University of Western Ontario Medical School. His subject was Recent Advances in the Field of Protein Nutrition.

Dr. Agnes Moffatt, Peterborough, Dr. Agnes White and Dr. Edna Guest of Toronto attended the sixth Congress of the Medical Women's International Association held in Philadelphia September 10 to 16. Members attended from Denmark, the Netherlands, Finland, France, Italy, China, Thailand, Yugo-Slavia and Great Britain. Dr. Guest, vice-president for Canada was made an honorary member of the Asssociation.

St. Joseph's Hospital, Hamilton has received a grant from the Federal Health Department of about $149,000 to assist with building room to provide 115 beds for maternity patients.

In Rainy River a new Red Cross hospital is being built to replace a smaller one, the new one will have 14 beds. Construction is to be assisted by a $15,000 federal grant.

The Muskoka Hospital for treatment of tuberculosis at Gravenhurst will be enlarged to provide space for 42 additional beds. A federal grant of $52,500 will be given for this.

LILLIAN A. CHASE

Quebec

A la séance d'ouverture du XXème Congrès de l'Association des Médecins de Langue Française du Canada, M. Hubert Guérin, ambassadeur de France au Canada, remit au nom de son pays les palmes académiques aux Drs Donatien Marion, Albert Jutras, Armand Frappier, et à M. Jules Labarre. Au cours de la soirée un diplôme d'honneur fut présenté aux Drs A. L. Richard, J. A. Lecours et J. E. Perras pour services insignes rendus à l'Association.

Les Drs Wilbrod Bonin et Roméo Pépin ont été élu respectivement doyen et vice-doyen de la Faculté de Médecine de l'Université de Montréal.

Le Dr Marcel Langlois a été nommé directeur médical de l'Hôtel-Dieu d'Edmundston, Nouveau-Brunswick. Gradué de Laval où il s'était distingué comme professeur et chef du département de pédiatrie à la Faculté de Médecine, le Dr Langlois occupait récemment le poste de directeur adjoint des études sur l'assurance-santé à Ottawa.

L'Hon. Albini Paquette, ministre de la Santé, inaugura le 1er octobre l'Hôtel-Dieu de St-Jérome, une construction de 9 étages des plus modernes qui pourra dès son ouverture hospitaliser quelque 152 malades.

Le Dr Gustave Gingras, directeur du service de médecine physique au ministère des Affaires des Anciens Combattants vient d'être nommé membre de l'American Board of Physical Medicine et de l'American Society of Physical Medicine. C'est le premier canadien à recevoir cet honneur.

Le Dr Jean Bernard, de la faculté de médecine de Paris, commence une série de cours cliniques et de conférences sur l'hématologie à l'Hôpital St-Luc.

Le Dr J. A. Denoncourt a été élu président du 21ième Congrès de l'Association des Médecins de Langue Française du Canada, qui sera tenu aux Trois-Rivières en 1951. Les Drs J. B. Jobin, J. M. Laframboise, Gustave Lacasse, sénateur, et Auray Fontaine en seront les vices-présidents. Le Dr Jos. Normand a été nommé secrétaire et le Dr J. L. Rochefort, trésorier.

Le nouveau comité d'Economie Médicale, qui s'occupe des intérêts professionnels des médecins, comprend les officiers suivants: Dr Emile Blain de Montréal, président; membres: Drs Armand Rioux et Pierre Jobin de Québec, Drs Roma Amyot et Conrad

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At a recent meeting of the College of Physicians and Surgeons of Quebec, the following officers were elected: President—Dr. Marc Trudel, Shawinigan; 1st Vice-president—Dr. J. F. A. Gatien, Montreal; 2nd Vice-president—Dr. R. Vance Ward, Montreal; 3rd Vice-president—Dr. Armand Beauchesne, Beauceville-Est; Registrar—Dr. Jean Paquin, Montreal; Governors—Drs. Paul R. Archambault, Montreal, J. Eugene Bissonnette, Quebec, Wilbrod Bonin, Montreal, Louis Couillard, Sorel, Arthur Fafard, Levis, Donald Fleming, Montreal, Georges A. Joubert, Priceville, L. P. Laporte, Montreal, Edouard Laverdure, Hull, Wilfrid Melançon, Drummondville, Jean Mercille, Montreal, J. Emile Phaneuf, St-Jean, Edmond Piette, Joliette, A. R. Potvin, Quebec, James Quintin, Sherbrooke, Armand Rioux, Quebec, Gerard Tremblay, Chicoutimi.

On September 28 a very pleasant ceremony took place to mark the conclusion of the Hospital Campaign in Montreal. This campaign was begun in May to raise funds for the Montreal General Hospital, the Children's Memorial Hospital and the Royal Edward Laurentian Hospital. The objective of the campaign was $18,000,000, the largest sum yet aimed at for such an object in Canada, and in the opinion of some it seemed too ambitious a project. However, the money has been duly raised, with an additional $200,000 as well clear of campaign expenses. The chairman of the campaign was Mr. Hartland Molson, and it was as a token of esteem for his leadership in the campaign that a group of friends gathered to present him with a painting by Robert Pilot, R.C.A. Mr. Molson, in acknowledging the gift, spoke of the generous support of the people of Montreal, and noted with pleasure also the part played by governmental agencies both provincial and municipal.

There were more than 200,000 donors on the records of the Fund, in addition to many anonymous gifts, and more than 9,000 volunteer workers canvassed for funds.

The sources of the money were as follows: governments 36%; corporations and employees 40%; personal gifts 22%; hospital staffs 2%. All costs of the campaign now stand at less than 1% of the money raised.

Plans are now being completed for the construction of the new hospital buildings for the Montreal General and the additions to the Children's Memorial and Royal Edward Laurentian Hospitals.

Saskatchewan

The City of Prince Albert and surrounding district have decided to become established as a health region for public health purposes.

At the MacNeill Psychiatric Clinic in Saskatoon, Dr. A. Stephen has taken over the post of Director in the place of Dr. Selinger. Dr. Selinger has left the Government service to enter private practice in the City of Saskatoon.

Dr. W. S. Alexander from New Zealand, a diplomate of the American Board of Pathology, has joined the staff of Grey Nuns' Hospital in Regina. Dr. Geoffrey Kent has come to the province to be pathologist at Moose Jaw, and he will be available to take over a lot of the work from the south-west corner of the province.

A committee has been established by the College of Physicians and Surgeons to make a study of the diagnostic and laboratory facilities of the province to be followed by recommendations concerning improvement in quantity, quality and availability. Dr. F. C. Heal, Moose Jaw is Chairman and members of the committee are Dr. C. J. Houston, Yorkton, Dr. L. G. Bray, Moose Jaw, Dr. A. J. Longmore, Regina, Dr. D. F. Moore, Saskatoon. Results of their study will be awaited with great interest.

Other new registrants in the province are Dr. J. Dillon at Grey Nuns' Hospital, Regina; Dr. A. F. Hildebrand, Beechy; Dr. Rosa Koslowsky, Prince Albert Sanatorium; Dr. M. B. Nestel, Foam Lake; and Dr. R. A. Stubbins, Bengough.

Changes within the province include Dr. W. Auerbach now practising at Pangman; Dr. G. M. Beall practising at Hafford; Dr. L. J. Genesove of Limerick now at Assiniboia; Dr. C. Hamwee formerly of Foam Lake to Melville; Dr. J. C. Lanskail of Hafford now on the instructing staff of the University of Saskatchewan.

Dr. W. A. Chestnut who had retired from practice at Moosomin, suffered painful injuries as a result of a car accident on the highway. G. G. FERGUSON

General

The University of Toronto, Faculty of Medicine, announces a combined Refresher Course in Ophthalmology and Otolaryngology during the week of January 29 to February 3, 1951. Dr. Phillips S. Thygeson, University of California School of Medicine and Dr. Charles E. Iliff, Johns Hopkins University will be guest speakers in Ophthalmology. Dr. LeRoy Schall, Harvard University and Dr. G. E. Tremble, McGill University will be guest speakers in Otolaryngology. There will be surgical and medical clinics in these two subjects in addition to lectures by members of the Faculty. The course will be given for a minimum of 10 students and a maximum of 25 students. Application may be made to the Dean of the Faculty of Medicine not later than November 30, 1950.

The Department of National Health and Welfare announces that an official invitation has been received for representation at an International Congress of Gynæcology organized by the French Gynæcological Society to be held in Paris from June 23 to 29, 1951. The Department does not propose to send an official delegation to this Congress, but the information regarding it is passed on for appropriate action in order that interested members of the profession wishing to attend the meeting on their own may be informed.

Book Reviews

B.C.G. Vaccination in Theory and Practice. K. N. Irvine, Medical Superintendent Smith Isolation Hospital; Physician to the Henley War Memorial Hospital. Foreword by K. Birkhaug, Chief of the B.C.G. Laboratory, New York State Department of Health. 130 pp. $4.00. Charles C. Thomas, Springfield, Illinois.

At the present time vaccination with B.C.G. for protection against tubercular infection is being practised in nearly every country in the world. Some countries, Norway and Sweden for example, have gone so far as to make vaccination compulsory for certain groups of people. Even on this continent where there is less confidence in its effectiveness B.C.G. vaccination is spreading rapidly. The literature on B.C.G. is very extensive and is becoming more so, but Dr. K. G. Irvine eases the burden in his recent review of the subject. The book is short, clear, concise, and easy to read. The abiding question of safety of the vaccine is satisfactorily answered. The question of resistance, particularly the degree of resistance conferred on man by the vaccine is not answered but that is because the answer is not yet here. The evidence is, however, set forth clearly. The chapter on technique of vaccination is very complete. Any physician interested in tuberculosis, can get valuable historical, theoretical, and practical information from this book.

Children with Mental and Physical Handicaps. J. E. Wallace Wallin, Visiting Professor of Clinical Psychology, Upsala College. 549 pp., ilust. $6.65. Prentice-Hall, Inc., New York, 1949.

This book is written in an authoritative, yet concise, understandable way, so that professional people, teachers, psychologists, etc., may have a better comprehension of the physical nature of the individual child. There is throughout an emphasis on assessment of the child's educability, on social training, and on the importance of patience and wise handling in protecting the child from complicating psychological problems. The main stress of this book, over half of the pages, deals in a most comprehensive way with the whole subject of mental defect. Having defined what comprises mental defect, Dr. Wallin describes the many varieties; the associated problems are minutely discussed, especially genetics, and psychological testing; the psychometric and projection tests in common use, their value and shortcomings and how to make the best use of them. In the second half of the book the special clinical types of mental defect are discussed individually, classified and made clear as entities in themselves. The importance of this identification of the type of defect is shown to be of great value for purposes of special treatment, to show the child's educational potentials, as well as the complexity of the problem of mental subnormality. Study of the special syndromes includes an approach to the whole problem of endocrinology. There are complete studies on the Mongol, the Nerve Degenerations, on Epilepsy, Encephalitis Lethargica, the Cerebral Palsies and Poliomyelitis. Psychological implications of motor defects in the child are emphasized. In all physically defective children as well as in those who are backward, conduct disorder and much vocational incompetence is shown to be due to the child's maladjustment to his life.

The value of this book to the doctor is in this psychological approach, which provides always the rounded conception of the handicapped child as a person, and his need for help in order that he may realize his highest development or best rehabilitation.

A History of Biology. C. Singer. 579 pp., illust. Revised ed. $5.00. Henry Schumann, Inc., New York 21, N.Y.

This is the revised edition of a work which was first published in 1931 and is a classic in the fields of science and history. Professor Singer has won for himself an eminence as a historian of science that is unrivalled today. He established his position in such works as *A Short History of Science* and *A Short History of Medicine* and it is once again a pleasure to acknowledge his mastery of the historical disciplines in this present work. With George Sarton and more recently with Professor Butterfield, Singer is providing an informed examination of the achievements of science which have brought into being the modern world, at the same time concerning himself with scientific thought and philosophy. Now that the progress of science has reached a turning point and with the breaking up of many of its stable foundations scientific thought finds itself driven to examine its philosophical bases and implications, Singer's expert charting of the scientific currents of the past assumes the greatest importance. Philosophers such as Whitehead in *Science and the Modern World* have indicated the tensions which exist, historians such as Singer have provided the detailed historical background, and with these materials it is now the contemporary task to resolve the conflicts which lie at the very heart of the present crisis in Christendom.

Professor Singer then is no mere chronicler of the discoveries of science. He is deeply concerned with the philosophy of science and presents the history of science as a bridge between natural science and the arts and thought of what has been called "our fractured civilization". In this history of the master science—biology—there is first a brilliant introduction dealing with the historical method in science. The narrative is divided into three sections: the older biology, the foundations of biology beginning with the seventeenth century, the biology of the last ninety years flowing in seven main channels.

Periodically in the course of the chronological development there are short and penetrating summaries, commentaries and single sentences throwing light on the matter under discussion and reminding the reader of the deeper implications involved. The writing is a model of its kind. Every page is informed with the judgment and knowledge of a historian of wide experience and wisdom. The format, printing and binding provided by Schumann are worthy of the writer. This is a distinguished book by a great teacher and historian.

Introduction to Neuropathology. S. P. Hicks, Department of Pathology of the Harvard Medical School and the New England Deaconess Hospital, Shields Warren, Departments of Pathology of the Harvard Medical School and the New England Deaconess Hospital. 494 pp., illust. $13.00. McGraw-Hill Co. of Canada, Ltd., 1950.

The authors have produced an easily-read and beautifully illustrated book. Their description of very early degenerative cortical changes, Page 7 *et seq.*, is difficult to appreciate and their photograph 1.26 on Page 32 is, in the reviewer's opinion, misleading. The important subject of intracranial aneurysms is inadequately dealt with and Fig. 227 on Page 101 is not the usual histological picture of an aneurysmal sac. The chapter on metabolic, toxic and degenerative changes is a very valuable and up-to-date description. Mechanical injuries are poorly dealt with. Tumours are well described and illustrated. Stress is laid on the very important group of tumours of the peripheral nervous system.

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Books Received

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Books are acknowledged as received, but in some cases reviews will also be made in later issues.

Foot Mechanics. For Chiropodists and students. L. R. Smart, S.R.N., M.CH.S. Chiropodist, Bermondsey and Southwark Group of Hospitals and Clinics, London. 106 pp., illust. $1.15. London: Baillière, Tindall and Cox, 7 and 8 Henrietta St., W.C.2. The Macmillan Co. of Canada Ltd., Toronto, 1950.

Recent Advances in Ocular Prosthesis. J. H. Prince. 155 pp., illust. $3.35. Edinburgh: E. & S. Livingstone Ltd., 16 and 17 Teviot Place. The Macmillan Company of Canada Ltd., Toronto, 1950.

Regional Dermatologic Diagnosis. A Practical System of Dermatology for the Non-specialist. E. Epstein, Consultant in Dermatology and Syphilology to the Oakland Area Veteran's Hospital and Mt. Zion Hospital. 328 pp., illust. $7.20. Lea & Febiger, Philadelphia. The Macmillan Company of Canada Ltd., Toronto, 1950.

Communicable Diseases. Edited by R. L. Pullen, Professor of Graduate Medicine, Director of the Division of Graduate Medicine, and Vice-Dean of the School of Medicine, Tulane University of Louisiana. 1035 pp., illust. $24.00. Lea & Febiger, Philadelphia. The Macmillan Company of Canada Ltd., Toronto, 1950.

Manual of Rheumatic Diseases. W. P. Holbrook and D. F. Hill. 182 pp., illust. $4.25. Year Book Publishers, Inc., 200 East Illinois St., Chicago, 1950.

Textbook of Gynæcology. A. H. Curtis, Emeritus Professor and Chairman of the Department of Obstetrics and Gynæcology, Northwestern University Medical School; and J. W. Huffman, Associate Professor of Obstetrics and Gynæcology, Northwestern University Medical School. 799 pp., illust. $11.50. W. B. Saunders Company, Philadelphia, Penna. McAinsh & Co. Limited, Toronto, 1950.

Office Treatment of the Nose, Throat and Ear. A. R. Hollender, Professor of Otolaryngology, Emeritus, University of Illinois College of Medicine. 620 pp., illust. $7.50. 3rd ed. Year Book Publishers, Inc., Chicago, 1950.

The Diagnosis of Salmonella Types. F. Kauffmann, International Salmonella Center, State Serum Institute, Copenhagen, Denmark. 86 pp. $3.00. Charles C. Thomas, Publisher, Springfield, Illinois. The Ryerson Press, Toronto, 1950.

The Scourge of Rheumatism. The Report of a Conference held by the British Rheumatic Association, London, September, 1949. 85 pp. 5s. net. William Heinmann, Medical Books Ltd., London, 1950.

Proceedings First National Conference on Cardiovascular Diseases, 1950. 259 pp. $1.75. Published June, 1950 by The American Heart Association, New York, N.Y., in co-operation with the National Heart Institute, U.S. Public Health Service, Federal Security Agency. International Press, New York, 1950.

The Treatment of Infections of the Hand. A 16 mm. sound and colour film, illustrating the practice of the Hand Clinic, University College Hospital, London. Surgeon in charge: R. S. Pilcher, Director of the Surgical Unit. Presented by the British Medical Association, Sponsored by Glaxo Laboratories, Greenford, Middlesex. 18 pp.

Statistical Year Book Quebec 1949. Published by authority of the Hon. Paul Beaubien, Minister of Trade and Commerce. 591 pp. Rédemti Paradis, Printer to the King's Most Excellent Majesty.

Vocational Rehabilitation of Psychiatric Patients. T. A. C. Rennie, Cornell University Medical College and the New York Hospital, Temple Burling and Luther E. Woodward, Division on Rehabilitation, the National Committee for Mental Hygiene. 133 pp. $.75. The Commonwealth Fund, New York, 1950.

Essential Urology. F. H. Colby, Chief of the Urological Service, Massachusetts General Hospital. 580 pp., illust. $9.00. The Williams & Wilkins Co., Baltimore; Burns & MacEachern, Toronto, 1950.

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Books Received

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Love is not Enough. B. Bettrlheim. The Treatment of Emotionally Disturbed Children. 386 pp., illust. $5.75. The Free Press, Glencoe, Illinois; Burns & MacEachern, Toronto, 1950.

Principles and Practice of Plastic Surgery. A. J. Barsky, Attending Plastic Surgeon, Beth Israel Hospital, New York City. 499 pp. $11.25. The Williams & Wilkins Co., Baltimore; Burns & MacEachern, Toronto, 1950.

The British Encyclopædia of Medical Practice. 2nd ed., under the Editorship of the Rt. Hon. Lord Horder, Extra Physician to H.M. The King, Consulting Physician to St. Bartholomew's Hospital, London. Vol. I, Abdominal Emergencies to Anus Diseases. 786 pp., illust. Butterworth & Co. (Publishers) Ltd., London, 1950.

Afecciones Cronicas de Los Ganglios Linfaticos del Cuello. L. R. Badia. 167 pp., illust. Administracion: Ediciones B Y P, Barcelona, 1950.

Lobotomia Frontal. A. Marti-Granell, y J. Usua Mariné. 99 pp. Coleccion Espanola de monografias Medicas. Administracion: Ediciones B Y P, Barcelona, 1950.

Studies in Lobotomy. M. Greenblatt, R. Arnot and H. C. Solomon, Editors. 495 pp., illust. $12.00. Grune & Stratton, Inc., New York; The Ryerson Press, Toronto, 1950.

Researches on the Radiotherapy of Oral Cancer. C. A. P. Wood and J. W. Boag. 148 pp., illust. 12s. 6d. net. Privy Council—Medical Research Council Special Report Series, No. 267. His Majesty's Stationery Office, London, 1950.

German Aviation Medicine, World War II. In 2 vols. Prepared under the auspices of the Surgeon General, U.S. Air Force, Department of the Air Force. Vol. 1, 648 pp.; Vol. 2, 1302 pp., illust. $8.50. U.S. Government Printing Office, Washington, D.C., 1950.

Principles of Ophthalmology. T. Henderson, Senior Surgeon Nottingham and Midland Eye Infirmary. 230 pp., illust. 20s. net. William Heinemann, Medical Books, Ltd., London, 1950.

Williams Obstetrics. N. J. Eastman, Professor of Obstetrics, Johns Hopkins University, and Obstetrician-in-chief to the Johns Hopkins Hospital. 1176 pp., illust. $12.50. Appleton-Century-Crofts, New York, 1950.

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